



# STIC SEARCH RESULTS

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher* or *contact:*

Mary Hale, Information Branch Supervisor  
308-4258, CM1-1E01

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop-off or send completed forms to STIC/Biotech-Chem Library CM1 - Circ. Desk



=> d his

(FILE 'HOME' ENTERED AT 15:17:42 ON 24 JUN 2003)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 15:17:54 ON 24 JUN 2003  
E METOPROLOL/CN

L1 1 S E3  
SEL RN  
L2 29 S E1/CRN  
L3 17 S L2 NOT MXS/CI  
L4 229 S C15H25NO3/MF AND 46.150.18/RID AND 1/NR  
L5 17 S L4 AND 2 PROPANOL AND 2 METHOXYETHYL PHENOXY  
L6 13 S L5 NOT (D OR T)/ELS  
L7 7 S L6 AND 4  
SEL RN  
L8 14 S E2-E8/CRN NOT L2  
L9 13 S L8 NOT MXS/CI  
L10 7 S L9 NOT COMPD  
L11 31 S L1,L3,L7,L10  
L12 22 S L11 NOT (COMPD OR WITH)  
L13 21 S L12 NOT 11C  
L14 10 S L11 NOT L13

FILE 'HCAPLUS' ENTERED AT 15:23:45 ON 24 JUN 2003

L15 2799 S L13  
L16 3247 S METOPROLOL OR BEATROLOL OR SPESICOR OR CGP2175 OR CGP 2175  
L17 3560 S L15,L16  
E ALEXANDER J/AU  
L18 320 S E3,E8-E10  
E ALEXANDER JOHN/AU  
L19 29 S E3,E10-E12  
E SCHUH J/AU  
L20 53 S E3,E6,E14,E17,E18,E21,E22  
L21 1 S L17 AND L18-L20

FILE 'REGISTRY' ENTERED AT 15:25:56 ON 24 JUN 2003

L22 1 S EPLERENONE/CN  
L23 36 S 107724-20-9/CRN

FILE 'HCAPLUS' ENTERED AT 15:27:15 ON 24 JUN 2003

L24 67 S L22  
L25 8 S L23  
L26 81 S EPLERENONE OR SC66110 OR SC() (66110 OR 66 110) OR CGP30083 OR  
L27 92 S L24-L26  
L28 7 S L27 AND L18-L20  
L29 1 S L21 AND L28  
L30 1 S US20020123485/PN  
E WO2001-US23670/AP, PRN  
L31 1 S E3,E4  
E US2000-221365/AP, PRN  
L32 1 S E5  
L33 1 S L29-L32  
SEL RN

FILE 'REGISTRY' ENTERED AT 15:29:09 ON 24 JUN 2003

L34 80 S E1-E80  
L35 2 S L34 AND L22,L23  
L36 1 S L34 AND L13  
L37 16 S L34 AND NR>=5  
L38 12 S L34 AND NR>=6  
L39 16 S L37,L38  
L40 63 S L34 NOT L35-L39

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
jan.delaval@uspto.gov

L41 3 S L39 AND K/ELS  
 L42 11 S L38 NOT L41  
 L43 10 S L42 AND 1/NC  
 L44 STR  
 L45 50 S L44  
 L46 STR L44  
 L47 18 S L46  
 L48 STR L46  
 L49 50 S L48  
 L50 SCR 1851  
 L51 50 S L48 AND L50  
 L52 1341 S L48 AND L50 FUL  
 SAV L52 QAZI917/A  
 L53 STR  
 L54 22 S L53 SAM SUB=L52  
 L55 10 S L34 AND L52  
 L56 6 S L39 NOT L55  
 L57 554 S L53 FUL SUB=L52  
 SAV L57 QAZI917A/A  
 L58 552 S L57 NOT (CCS OR RIS OR PMS)/CI

FILE 'HCAPLUS' ENTERED AT 15:52:30 ON 24 JUN 2003

L59 67 S L55  
 L60 4 S L59 AND L17

FILE 'REGISTRY' ENTERED AT 15:53:12 ON 24 JUN 2003

L61 5 S L56 NOT C24H32O4S

FILE 'HCAPLUS' ENTERED AT 15:53:50 ON 24 JUN 2003

L62 2 S L61  
 L63 1 S L62 AND L17  
 L64 4 S L27 AND L17  
 L65 4 S L33,L60,L63,L64  
 L66 360 S L58  
 L67 4 S L66 AND L17  
 L68 4 S L65,L67

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:56:48 ON 24 JUN 2003  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JUN 2003 HIGHEST RN 536496-82-9  
 DICTIONARY FILE UPDATES: 23 JUN 2003 HIGHEST RN 536496-82-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

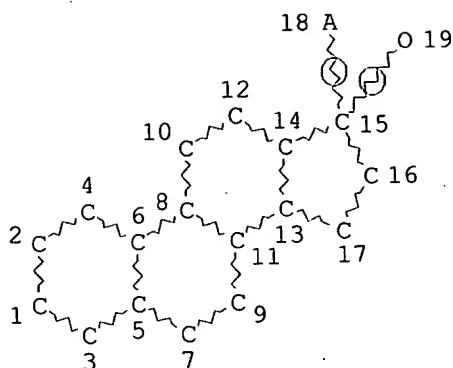
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
 PROPERTIES for more information. See STNote 27, Searching Properties  
 in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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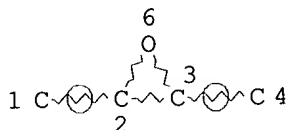
L48 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE  
 L50 SCR 1851  
 L52 1341 SEA FILE=REGISTRY SSS FUL L48 AND L50  
 L53 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 5

STEREO ATTRIBUTES: NONE  
 L57 554 SEA FILE=REGISTRY SUB=L52 SSS FUL L53

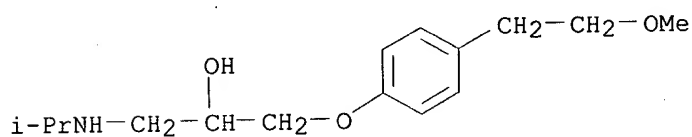
100.0% PROCESSED 607 ITERATIONS  
 SEARCH TIME: 00.00.01

554 ANSWERS

=> d ide can ll

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS  
 RN 51384-51-1 REGISTRY  
 CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)  
 (CA INDEX NAME)  
 OTHER NAMES:  
 CN (.+-.)-Metoprolol  
 CN (RS)-Metoprolol  
 CN 1-Isopropylamino-3-[4-(2-methoxyethyl)phenoxy]-2-propanol  
 CN Beatrolol  
 CN CGP 2175  
 CN dl-Metoprolol

CN **Metoprolol**  
 CN Spesicor  
 FS 3D CONCORD  
 DR 54163-88-1, 37350-58-6  
 MF C15 H25 N O3  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,  
 CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, HSDB\*,  
 IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, NIOSHTIC, PHAR,  
 PHARMASEARCH, PROMT, RTECS\*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2,  
 USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

2327 REFERENCES IN FILE CA (1957 TO DATE)  
 29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 2329 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:406708  
 REFERENCE 2: 138:396171  
 REFERENCE 3: 138:395842  
 REFERENCE 4: 138:378918  
 REFERENCE 5: 138:378518  
 REFERENCE 6: 138:378466  
 REFERENCE 7: 138:373982  
 REFERENCE 8: 138:362715  
 REFERENCE 9: 138:362688  
 REFERENCE 10: 138:362127

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L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS  
 RN 107724-20-9 REGISTRY  
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
 .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA  
 INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Spiro[9,11-epoxy-9H-cyclopenta[a]phenanthrene-17(2H),2'(3'H)-furan],

pregn-4-ene-7,21-dicarboxylic acid deriv.

## OTHER NAMES:

CN CGP 30083

CN **Eplerenone**

CN SC 66110

FS STEREOSEARCH

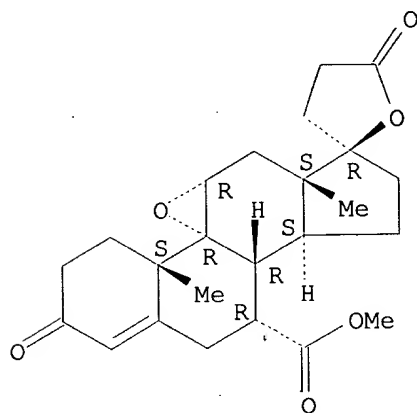
MF C24 H30 O6

CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

67 REFERENCES IN FILE CA (1957 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

69 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:395116

REFERENCE 2: 138:363210

REFERENCE 3: 138:362110

REFERENCE 4: 138:343856

REFERENCE 5: 138:335571

REFERENCE 6: 138:296950

REFERENCE 7: 138:202478

REFERENCE 8: 138:163269

REFERENCE 9: 138:134888

REFERENCE 10: 138:126982

=> fil hcaplus  
 FILE 'HCAPLUS' ENTERED AT 15:57:22 ON 24 JUN 2003  
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FILE COVERS 1907 - 24 Jun 2003 VOL 138 ISS 26  
 FILE LAST UPDATED: 23 Jun 2003. (20030623/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L68 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2003 ACS  
 AN 2003:319257 HCAPLUS  
 DN 138:343856  
 TI Buccal sprays or capsules containing cardiovascular or renal drugs  
 IN Dugger, Harry A.  
 PA USA  
 SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 537,118.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 IC ICM A61K009-00  
 ICS A61L009-04  
 NCL 424043000  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003077229	A1	20030424	US 2002-230075	20020829
	WO 9916417	A1	19990408	WO 1997-US17899	19971001
	W:				
	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
	DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,				
	LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,				
	PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,				
	UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,				
	GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,				
	GN, ML, MR, NE, SN, TD, TG				
	EP 1029536	A1	20000823	EP 2000-109347	19971001
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
	EP 1036561	A1	20000920	EP 2000-109357	19971001
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
PRAI	WO 1997-US17899	A2	19971001		
	US 2000-537118	A2	20000329		
	EP 1997-911621	A3	19971001		
AB	Buccal aerosol sprays or capsules using polar and non-polar solvent have				

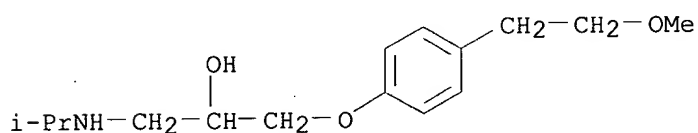
now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aq. polar solvent, active compd., and optional flavoring agent; formulation B: aq. polar solvent, active compd., optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compd., and optional flavoring agent; and formulation D: non-polar solvent, active compd., optional flavoring agent, and propellant. Thus, a polar lingual spray contained isoproterenol-HCl 0.5-6, water 50-75, EtOH 5-10, PEG 5-15, sorbitol 0.4-1.0, aspartame 0.04-0.1, and flavors 2-3%.

- ST cardiovascular drug buccal spray; renal drug capsule
- IT Fatty acids, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (C2-24; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Alcohols, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (C2-8; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Alcohols, biological studies  
 Hydrocarbons, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (C7-18; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Drug delivery systems  
 (aerosols, sprays; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Antianginal agents  
 Antiarrhythmics  
 Anticoagulants  
 Antihypertensives  
 Antihypotensives  
 Cardiovascular agents  
 Flavor  
 Polar solvents  
 Propellants (sprays and foams)  
 Sweetening agents  
 Vasodilators  
 (buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Esters, biological studies  
 Glycerides, biological studies  
 Pentosans  
 Polyoxyalkylenes, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Drug delivery systems  
 (buccal; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Drug delivery systems  
 (capsules; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Essential oils  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (citrus; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Heart, disease  
 (failure; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Flavoring materials  
 (fruit flavors; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Mucopolysaccharides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (heparinoids; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Peptides, biological studies.



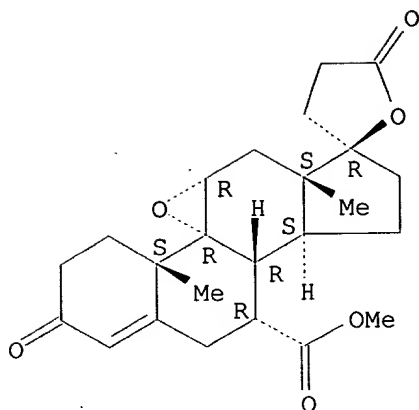
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hormones; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Mouth  
(mucosa; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Drug delivery systems  
(mucosal; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peppermint; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Hormones, animal, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptide; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Alcohols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyhydric, C2-8; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Heart  
(regulators for; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(spearmint; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT Drug delivery systems  
(sprays; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT 9005-49-6, Heparin, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(SNAC/SNAD; buccal sprays or capsules contg. cardiovascular or renal drugs)
- IT 50-78-2, Aspirin 51-06-9, Procainamide 51-30-9, Isoproterenol hydrochloride 54-31-9, Furosemide 56-54-2, Quinidine 57-41-0, Phenytoin 58-00-4, Apomorphine 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies 59-41-6, Bretylium 60-87-7, Promethazine 64-17-5, Ethanol, biological studies 65-28-1, Phentolamine mesylate 71-63-6, Digitoxin 74-98-6, Propane, biological studies 75-28-5, Iso-butane 78-11-5, Pentaerythritol tetranitrate 78-78-4, Iso-pentane 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 89-25-8, Edaravone 106-97-8, N-Butane, biological studies 109-66-0, N-Pentane, biological studies 114-07-8, Erythromycin 127-31-1, Fludrocortisone 137-58-6, Lidocaine 147-24-0, DiPhenhydramine hydrochloride 303-53-7, Cyclobenzaprine 364-98-7, Diazoxide 463-04-7, Amyl nitrite 463-82-1, Neo-pentane 523-87-5, Dimenhydrinate 525-66-6, Propranolol 541-15-1, Carnitine 555-30-6, Methyldopa 569-65-3, Meclizine 630-93-3, Phenytoin sodium 745-65-3, Alprostadil 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 3737-09-5, Disopyramide 3930-20-9, Sotalol 4205-90-7, Clonidine 5786-21-0, Clozapine 6493-05-6, Pentoxifylline 7297-25-8, Erythrityl tetranitrate 9041-08-1 10238-21-8, Glyburide 13523-86-9, Pindolol 15078-28-1, Nitroprusside 19216-56-9, Prazosin 20830-75-5, Digoxin 21829-25-4, Nifedipine 23031-25-6, Terbutaline 23031-32-5, Terbutaline sulfate 25322-68-3, Polyethylene glycol 25717-80-0, Molsidomine 28395-03-1, Bumetanide 29110-47-2, Guanfacine 29122-68-7, Atenolol 30236-31-8, D-Sotalol 30516-87-1, Zidovudine 31329-57-4, Naftidrofuryl 31828-71-4, Mexiletine 34368-04-2, Dobutamine 35700-23-3, Carboprost 36894-69-6, Labetalol 37270-89-6, Nadroparin calcium 37517-30-9, Acebutolol 38304-91-5, Minoxidil 39562-70-4, Nitrendipine

41708-72-9, Tocainide 42200-33-9, Nadolol 42399-41-7, Diltiazem  
 42794-76-3, Midodrine 47931-85-1, Salmon calcitonin 49562-28-9,  
 Fenofibrate **51384-51-1, Metoprolol** 54063-53-5,  
 Propafenone 54143-55-4, Flecainide 55142-85-3, Ticlopidine  
 55837-25-7, Buflomedil 55985-32-5, Nicardipine 56211-40-6, Torsemide  
 56980-93-9, Celiprolol 62571-86-2, Captopril 63590-64-7, Terazosin  
 63659-18-7, Betaxolol 63675-72-9, Nisoldipine 64706-54-3, Bepridil  
 65141-46-0, Nicorandil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol  
 67227-56-9, Fenoldopam 70059-30-2, Cimetidine hydrochloride  
 72509-76-3, Felodipine 72956-09-3, Carvedilol 73963-72-1, Cilostazol  
 74191-85-8, Doxazosin 74863-84-6, Argatroban 75438-57-2, Moxonidine  
 75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril  
 76824-35-6, Famotidine 78415-72-2, Milrinone 78919-13-8, Iloprost  
 79517-01-4, Octreotide acetate 81147-92-4, Esmolol 81403-80-7,  
 Alfuzosin 82956-11-4, Nafamostat mesilate 83647-97-6, Spirapril  
 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril  
 87679-37-6, Trandolapril 88069-67-4, Pilsicainide 88150-42-9,  
 Amlodipine 88768-40-5, Cilazapril 89226-50-6, Manidipine 89371-37-9,  
 Imidapril 93107-08-5, Ciprofloxacin hydrochloride 95635-55-5,  
 Ranolazine 98048-97-6, Fosinopril 99614-01-4, Ondansetron  
 hydrochloride 100427-26-7, Lercanidipine 103628-48-4, Sumatriptan  
 succinate 103775-10-6, Moexipril 104713-75-9, Barnidipine  
 104993-28-4, Fondaparinux 106133-20-4, Tamsulosin 107133-36-8,  
 Perindopril erbumine **107724-20-9, Eplerenone**  
 110101-66-1, Tirilazad 113665-84-2, Clopidogrel 114798-26-4, Losartan  
 115256-11-6, Dofetilide 116308-55-5, Vatanidipine 120993-53-5,  
 Desirudin 125926-17-2, Sarpogrelate 128270-60-0, Bivalirudin  
 133040-01-4, Eprosartan 133107-64-9, Insulin lispro 137862-53-4,  
 Valsartan 138068-37-8, Lepirudin 138402-11-6, Irbesartan  
 139481-59-7, Candesartan 139755-83-2, Sildenafil 141505-33-1,  
 Levosimendan 143653-53-6, Abciximab 144494-65-5, Tirofiban  
 144701-48-4, Telmisartan 147536-97-8, Bosentan 159138-80-4, Cariporide  
 159776-70-2, Melagatran 166518-60-1, Avasimibe 167305-00-2,  
 Omapatrilat 168626-94-6, YM087 171596-29-5, Tadalafil 180384-57-0,  
 Tezosentan 188627-80-7, Eptifibatide 192939-46-1, H376/95  
 224785-90-4, Vardenafil 516482-86-3, Sermorelin acetate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (buccal sprays or capsules contg. cardiovascular or renal drugs)  
 IT **51384-51-1, Metoprolol 107724-20-9,**  
**Eplerenone**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (buccal sprays or capsules contg. cardiovascular or renal drugs)  
 RN 51384-51-1 HCAPLUS  
 CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)  
 (CA INDEX NAME)



RN 107724-20-9 HCAPLUS  
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
 .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:755214 HCAPLUS

DN 137:263024

TI Preparation of N-isoxazolyl biphenylsulfonamides and related compounds as dual angiotensin II and endothelin receptor antagonists.

IN Murugesan, Natesan; Tellev, John E.; Macor, John E.; Gu, Zhengxiang

PA USA

SO U.S. Pat. Appl. Publ., 206 pp., Cont.-in-part of U.S. Ser. No. 643,640, abandoned.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-4166

ICS A61K031-4184; A61K031-4196; C07D233-32; C07D213-68; C07D215-233; C07D249-08

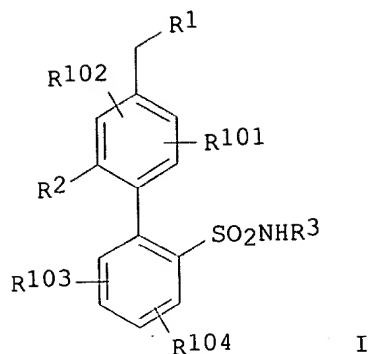
NCL 514258000

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002143024	A1	20021003	US 2000-737201	20001214
PRAI	US 1998-91847P	P	19980706		
	US 1999-345392	B2	19990701		
	US 1999-464037	B2	19991215		
	US 2000-481197	B2	20000111		
	US 2000-513779	A2	20000225		
	US 2000-604322	A2	20000626		
	US 2000-643640	B2	20000822		
OS	MARPAT 137:263024				
GI					



- AB Title compds. (I; R1 = specified oxoimidazolyl, pyridoimidazolyl, pyridylamino, pyridyloxy, triazolyl, quinolinyl, etc.; R2 = H, halo, CHO, (halo)alkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxy, cyano, OH, NO<sub>2</sub>, etc.; R3 = heteroaryl; R101-R104 = H, halo, CHO, alkyl, haloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, cyano, OH, hydroxyalkyl, NO<sub>2</sub>, etc; with provisos) were prepd. as dual angiotensin II and endothelin receptor antagonists for treatment of hypertension and other diseases (no data). Thus, 4-BrC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>OH was coupled with [2-[(4,5-dimethyl-3-isoxazolyl)](2-methoxyethoxy)methyl]amino)sulfonyl]phenyl]boronic acid to give N-(4,5-dimethyl-3-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl][1,1'-biphenyl]-2-sulfonamide (66%). This was brominated to give the 4'-bromomethyl deriv. (90%), reacted with 2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one hydrochloride, and deprotected (49% for two steps) to give 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-[1,1'-biphenyl]-2-sulfonamide.
- ST isoxazolyl biphenylsulfonamide prepn angiotensin endothelin receptor antagonist; diazaspirononemethylmethylisoxazolylbiphenylsulfonamide prepn angiotensin endothelin receptor antagonist; antihypertensive biphenylsulfonamide prepn
- IT Angiotensin receptors  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
 (angiotensin II, antagonists; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Endothelin receptors  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
 (antagonists; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Antiarteriosclerotics  
 (antiatherosclerotics; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Prostate gland, disease  
 (benign hyperplasia, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Meninges  
 (disease, subarachnoid hemorrhage, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Sexual behavior  
 (disorder, treatment of female; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and

- endothelin receptor antagonists)
- IT Heart, disease  
Kidney, disease  
(failure, treatment; prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Sexual behavior  
(impotence, treatment; prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Antiasthmatics  
Antihypertensives  
Antimigraine agents  
Antitumor agents  
Human  
(prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Growth inhibitors, animal  
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Artery, disease  
(restenosis, treatment; prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT Atherosclerosis  
Endotoxemia  
Hypertension  
Ischemia  
(treatment; prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT 62571-86-2, Captopril 74258-86-9, Alacepril 75847-73-3, Enalapril 76547-98-3, Lisinopril 81872-10-8, Zofenopril 82924-03-6, Pentopril 83435-66-9, Delapril 85441-61-8, Quinapril 87333-19-5, Ramipril 98048-97-6, Fosinopril 111223-26-8, Ceranapril 160135-92-2, Gemopatrilat 167305-00-2, Omapatrilat  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; prepn. of N-isoxazolyyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)
- IT 254737-84-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyyl)-254737-85-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyyl)-2'-[(methylamino)methyl]-254737-86-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyyl)-2'-formyl-254737-87-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-254737-88-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyyl)-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]-254737-89-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-pyrazinyl-254737-90-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3-chloropyrazinyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-254737-91-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyyl)-2'-[(2-oxo-1-pyrrolidinyl)methyl]-254737-92-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-

dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-(3,6-dimethylpyrazinyl)-  
254737-94-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl]-N-(3-methoxypyrazinyl)- 254737-96-7P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-formyl- 254737-98-9P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-oxo-1-  
pyrrolidinyl)methyl]- 254738-00-6P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-  
5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-  
1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]- 254738-03-9P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-  
dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-  
imidazo[4,5-b]pyridin-3-yl)methyl]- 254738-05-1P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[[2-(2-methoxyethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-  
yl]methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-06-2P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-  
(ethoxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-  
254738-07-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(2-oxo-  
1-pyrrolidinyl)methyl]- 254738-09-5P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-  
b]pyridin-3-yl)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]-  
254738-10-8P, Pentanamide, N-[[2'-[[[(3-methyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-  
[(methylamino)carbonyl]propyl]- 254738-11-9P, Pentanamide,  
N-[[2'-[[[(4-bromo-3-methyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-  
yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-  
254738-12-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-  
propyl- 254738-13-1P, 1H-Benzimidazole-7-carboxylic acid,  
1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-  
yl]methyl]-2-ethoxy-, methyl ester 254738-14-2P, 1H-Benzimidazole-7-  
carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-4-yl]methyl]-2-ethoxy- 254738-15-3P, 1H-Benzimidazole-7-  
carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-4-yl]methyl]-2-ethyl-, methyl ester 254738-16-4P,  
1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-  
254738-17-5P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-, methylester  
254738-18-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- 254738-19-7P,  
1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N-methyl-  
254738-20-0P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N,N-dimethyl-  
254738-21-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-ethyl-4-  
quinolinyl)oxy]methyl]-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)- 254738-22-2P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-  
imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-23-3P,  
1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl-, methyl  
ester 254738-24-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N,N-  
dimethyl-2-propyl- 254738-25-5P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-(hydroxymethyl)- 254738-26-6P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-

en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(ethoxymethyl)-  
254738-27-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-  
methoxyethyl)- 254738-28-8P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-  
dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-(3-methoxy-5-methylpyrazinyl)-  
254738-29-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4-bromo-3-methyl-5-  
isoxazolyl)-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-  
[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254738-30-2P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-  
[(formylmethylamino)methyl]- 254738-31-3P, Propanamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-32-4P, Cyclopropanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-33-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-N,2-dimethyl- 254738-34-6P, Butanamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-35-7P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-2-methoxy-N-methyl- 254738-36-8P, 4-Pentynamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-37-9P, Cyclobutanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-38-0P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-N,3-dimethyl- 254738-39-1P, Propanamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,2,2-  
trimethyl- 254738-40-4P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-methoxy-N-methyl-  
254738-41-5P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-  
3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-2-ethoxy-N-methyl- 254738-42-6P,  
2-Furancarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-  
yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-  
2-yl)methyl]-N-methyl- 254738-43-7P, Pentanamide, N-[[4-[(2-butyl-4-oxo-  
1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,4-dimethyl-  
254738-44-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-  
3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-N-methyl- 254738-45-9P, 3-Thiophenecarboxamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-46-0P, Cyclopentaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-47-1P, Cyclohexanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-48-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-  
3-yl)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-2-yl)methyl]-N,3-dimethyl- 254738-49-3P, Benzeneacetamide,  
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-  
254738-50-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-

en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-fluoro-N-methyl- 254738-51-7P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-fluoro-N-methyl- 254738-52-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-fluoro-N-methyl- 254738-53-9P, Cyclohexaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-54-0P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-fluoro-N-methyl- 254738-55-1P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-fluoro-N-methyl- 254738-56-2P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-fluoro-N-methyl- 254738-57-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(dimethylamino)carbonyl)methylamino)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-58-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(1,1-dimethylethyl)amino)carbonyl)methylamino)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-59-5P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]methyl-, ethyl ester 254738-60-8P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]methyl-, 2-methylpropyl ester 254738-61-9P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3,3-trimethyl- 254738-62-0P, 2-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-63-1P, 3-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-64-2P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-65-3P, 1H-Pyrrole-2-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,1-dimethyl- 254738-66-4P, 1,2,3-Thiadiazole-4-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-67-5P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,5-dimethyl- 254738-68-6P, 4-Isioxazolecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3,5-trimethyl- 254738-69-7P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3-dimethyl- 254738-70-0P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,5-dimethyl- 254738-71-1P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-cyano-N-methyl- 254738-72-2P, Benzamide,



N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-cyano-N-methyl- 254738-73-3P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-methoxy-N-methyl- 254738-74-4P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-chloro-N-methyl- 254738-75-5P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-chloro-N-methyl- 254738-76-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-chloro-N-methyl- 254738-78-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2,3-difluoro-N-methyl- 254738-79-9P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3,4-difluoro-N-methyl- 254738-80-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3,5-difluoro-N-methyl- 254738-81-3P, Benzamide, 4-acetyl-N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254738-82-4P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-ethoxy-N-methyl- 254738-83-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-84-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(propylsulfonyl)amino]- 254738-85-7P, L-Valine, N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-(1-oxopentyl)-methyl ester 254738-86-8P, L-Valine, N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-(1-oxopentyl)- 254738-87-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(4-oxo-2-propyl-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254738-88-0P, Butanamide, N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl)methyl]-N,3,3-trimethyl- 254738-89-1P, Pentanamide, N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254738-90-4P, Pentanamide, N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254738-91-5P, Pentanamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254738-92-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[[2,2,2-trifluoroethyl)amino)methyl]- 254738-93-7P, [1,1'-Biphenyl]-2-carboxylic acid, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]- 254738-94-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(trifluoromethyl)- 254738-95-9P, [1,1'-Biphenyl]-2-carboxylic acid, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-, methyl ester 254738-96-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(methoxymethyl)- 254738-97-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro- 254738-98-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-

3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254738-99-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-  
254739-00-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)- 254739-01-0P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-methyl- 254739-02-1P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254739-03-2P,  
Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-04-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[[2,2,2-trifluoroethyl)amino]methyl]- 254739-05-4P, Benzeneacetamide,  
N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]- 254739-06-5P, Butanamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]-3,3-dimethyl-  
254739-07-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-amino-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-08-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-nitro- 254739-09-8P, Pentanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-10-1P, Cyclopropanecarboxamide,  
N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-11-2P, Benzenepropanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-12-3P, Pentanamide,  
2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-13-4P, Hexanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-14-5P, Pentanamide,  
2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-15-6P, Pentanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,4-dimethyl-, (2S)- 254739-16-7P, Cyclopropanecarboxamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-17-8P, Benzenepropanamide,  
N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-18-9P, Benzeneacetamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-19-0P, Pentanamide,  
2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254739-20-3P, Hexanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-21-4P, Pentanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254739-22-5P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S)- 254739-23-6P, Cyclopropanecarboxamide,  
N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-24-7P, Benzenepropanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-

[(methylamino)carbonyl]propyl]- 254739-25-8P, Benzeneacetamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254739-26-9P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-27-0P, Hexanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254739-28-1P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-29-2P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(ethylamino)carbonyl]-2-methylpropyl]-254739-30-5P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(hexylamino)carbonyl]-2-methylpropyl]-254739-31-6P, Pentanamide, N-[[2-cyano-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254739-32-7P, Pentanamide, N-[[2-(cyanomethyl)-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254739-33-8P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-254739-34-9P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-N,N-dimethyl-254739-35-0P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-N-methyl-254739-36-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(methoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254739-37-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-methyl-254739-38-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-methyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254739-39-4P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-40-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(hydroxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254739-41-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]-254739-42-9P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-fluoro[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-43-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(phenoxymethyl)-254739-44-1P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(1H-pyrazol-1-yl)methyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-45-2P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-254739-46-3P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)- 254739-47-4P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-254739-48-5P, Butanamide, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)- 254739-49-6P, Pentanamide, N-[[2-chloro-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254739-50-9P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-

[(methylamino)carbonyl]propyl]- 254739-51-0P, Cyclobutanecarboxamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-52-1P, 1H-Imidazole-5-carboxylic acid, 1-[[2-chloro-2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl]- 254739-53-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(methylsulfonyl)amino]- 254739-54-3P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(4-methyl-1-piperazinyl)carbonyl]propyl]- 254739-55-4P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-(1-piperidinylcarbonyl)propyl]- 254739-56-5P, Pentanamide, N-[(1S)-1-[[[(3,3-dimethylbutyl)amino]carbonyl]-2-methylpropyl]-N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254739-57-6P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-methylpropyl]- 254739-58-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(1-methylethoxy)methyl]-  
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)  
 IT 254739-59-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(propoxymethyl)- 254739-60-1P, 1H-Imidazole-5-carboxamide, 4-chloro-1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl]- 254739-61-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-62-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-oxo-1(2H)-pyridinyl)methyl]- 254739-63-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(1H-pyrazol-1-yl)methyl]- 254739-64-5P, 1H-Imidazole-5-carboxamide, 2-butyl-4-chloro-1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254739-65-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-methyl-4-quinolinyl]oxy]methyl]- 254739-66-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-ethyl-4-quinolinyl]oxy]methyl]- 254739-67-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl]oxy]methyl]- 254739-68-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-propyl-4-quinolinyl]oxy]methyl]- 254739-69-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(6,7-dihydro-2,4-dimethyl-7-oxopyrido[2,3-d]pyrimidin-8(5H)-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-70-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[2-ethyl-4-quinolinyl]oxy]methyl]- 254739-71-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl]oxy]methyl]- 254739-72-5P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-N-methyl- 254739-73-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, phenylmethyl ester 254739-74-7P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 2-phenylethyl ester 254739-75-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-

yl)methyl]-2-ethyl-, 2-(2-oxo-1-pyrrolidinyl)ethyl ester 254739-76-9P,  
1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-,  
3-(2-oxo-1-pyrrolidinyl)propyl ester 254739-77-0P, [1,1'-Biphenyl]-2-  
sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-ethyl-4-  
quinolinyl)oxy]methyl]- 254739-79-2P, [1,1'-Biphenyl]-2-sulfonamide,  
2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-  
oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-80-5P,  
1H-Imidazole-5-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-  
propyl- 254739-81-6P, 1H-Imidazole-5-carboxamide, 1-[[2-chloro-2'-[[[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-  
2-propyl- 254739-82-7P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[(3,4-  
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-  
2-propyl- 254739-83-8P, 1H-Benzimidazole-7-carboxamide,  
1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-  
yl)methyl]-2-ethoxy-N-methyl- 254739-84-9P, 1H-Benzimidazole-7-  
carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-  
biphenyl]-4-yl)methyl]-2-ethoxy-N,N-dimethyl- 254739-85-0P,  
3-Pyridinecarboxylic acid, 2-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]propylamino]-  
254739-86-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-  
triazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-87-2P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-  
tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-  
254739-88-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2,7-diethyl-5H-  
pyrazolo[1,5-b][1,2,4]triazol-5-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-  
254739-89-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-butyl-6-[[[methyl(1-  
methylethyl)amino]carbonyl]amino]-4-oxo-3(4H)-quinazolinyl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)- 254739-90-7P, 3-Pyridinecarboxamide,  
2-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-  
yl)methyl]propylamino]-N-methyl- 254739-91-8P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-  
pyridinyl)oxy]methyl]- 254739-92-9P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl]-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-  
254739-93-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(5,6,7,8-tetrahydro-8-  
oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-94-1P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[3-  
methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(methoxymethyl)-  
254739-95-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-4-methyl-  
254739-96-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-3(4H)-  
quinazolinyl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-97-4P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl]- 254739-98-5P, Pentanamide, N-[[2'-[[[(3,4-dimethyl-  
5-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-  
[(methylamino)carbonyl]propyl]- 254739-99-6P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(4,4-dimethyl-2-oxo-1-  
pyrrolidinyl)methyl]- 254740-00-6P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(3,4-dimethyl-5-  
isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-  
254740-01-7P, Acetamide, N-[2'-[[2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-  
b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl)methyl]methylamino]ethyl]-  
254740-02-8P, [1,1'-Biphenyl]-2-acetic acid, 2'-[[[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-  
b]pyridin-3-yl)methyl]-, ethyl ester 254740-03-9P, Pentanamide,  
N-[[2'-[[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-

yl)methyl]-N-[(1S)-2-methyl-1-[(propylamino)carbonyl]propyl]-  
254740-04-0P, Pentanamide, N-[[2'-[(3,4-dimethyl-5-  
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-  
[[[tetrahydro-2-furanyl)methyl]amino]carbonyl]propyl]- 254740-05-1P,  
[1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-  
[[2-ethyl-4-quinolinyl)oxy]methyl]- 254740-06-2P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-ethyl-4-  
quinolinyl)oxy]methyl]-2'-(trifluoromethyl)- 254740-07-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)- 254740-08-4P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-methylpropoxy)methyl]-  
254740-09-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-  
[(ethylsulfonyl)amino]- 254740-10-8P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-[(2,2,2-trifluoroethoxy)methyl]- 254740-11-9P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-  
254740-12-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
2'-(ethoxymethyl)-4'-[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-  
254740-15-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
2'-(ethoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-  
cycloheptimidazolyl)methyl]- 254740-18-6P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(3,4-dimethyl-5-isoxazolyl)-2'-(3,3,3-trifluoropropyl)- 254740-20-0P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-  
254740-21-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(1,1-difluoroethyl)-N-(3,4-  
dimethyl-5-isoxazolyl)- 254740-22-2P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-(2,2,2-trifluoroethyl)- 254740-23-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-methylpropoxy)-  
254740-24-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-  
methoxyethoxy)- 254740-25-5P, [1,1'-Biphenyl]-2-sulfonamide,  
2'-butyl-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(3,4-dimethyl-5-isoxazolyl)- 254740-26-6P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)- 254740-27-7P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(4-bromo-3-methyl-5-isoxazolyl)-4'-[(2-  
butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(trifluoromethyl)-  
254740-28-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4-chloro-3-methyl-5-isoxazolyl)-2'-  
(trifluoromethyl)- 254740-29-9P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-[(methoxymethylamino)methyl]- 254740-30-2P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-[(2,2-difluoroethoxy)methyl]-N-(3,4-dimethyl-5-  
isoxazolyl)- 254740-31-3P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-(2-fluoroethyl)- 254740-32-4P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-hydroxyethyl)-  
254740-33-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-  
methylbutyl)- 254740-34-6P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-(2-methylpropyl)- 254740-35-7P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(3,3-difluorobutyl)-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-

(ethoxymethyl)- 254740-36-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[ (3-methoxy-2,6-dimethyl-4-pyridinyl)oxy)methyl]-2'-(3,3,3-trifluoropropyl)- 254740-37-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254740-38-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[ (3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254740-39-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[ (3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254740-40-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[ (3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254740-41-5P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[ (3,4-dimethyl-5-isoxazolyl)amino)sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254740-42-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(methoxylamino)methyl]- 254740-43-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254740-44-8P, Pentanamide, N-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]- 254740-45-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254740-46-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[2-(2-methoxyethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254740-47-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[2-(ethoxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254740-48-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(2-oxo-1-pyrrolidinyl)methyl]- 254740-49-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254740-50-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl- 254740-51-7P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-, methyl ester 254740-52-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy- 254740-53-9P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-, methyl ester 254740-54-0P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl- 254740-55-1P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-, methylester 254740-56-2P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy- 254740-57-3P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-N-methyl- 254740-58-4P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-N,N-dimethyl- 254740-59-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-ethyl-4-quinolinyl)oxy)methyl]-N-(3-methyl-5-isoxazolyl)- 254740-60-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-imidazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-61-9P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[ (4,5-dimethyl-3-



isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-propyl-, methyl ester 254740-62-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N,N-dimethyl-2-propyl- 254740-63-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(hydroxymethyl)- 254740-64-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)- 254740-65-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methoxyethyl)- 254740-66-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(formylmethylamino)methyl]- 254740-67-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-68-6P, Cyclopropanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-69-7P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,2-dimethyl- 254740-70-0P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-71-1P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-methoxy-N-methyl- 254740-72-2P, 4-Pentynamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-73-3P, Cyclobutanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-74-4P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3-dimethyl- 254740-75-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,2,2-trimethyl- 254740-76-6P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-methoxy-N-methyl- 254740-77-7P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-ethoxy-N-methyl- 254740-78-8P, 2-Furancarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-79-9P, Pentanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,4-dimethyl- 254740-80-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-81-3P, 3-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-82-4P, Cyclopentaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-83-5P, Cyclohexanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3-dimethyl- 254740-85-7P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl-



254740-86-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-fluoro-N-methyl- 254740-87-9P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-fluoro-N-methyl- 254740-88-0P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-fluoro-N-methyl- 254740-89-1P, Cyclohexanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-90-4P, Benzenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-fluoro-N-methyl- 254740-91-5P

, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-fluoro-N-methyl- 254740-92-6P, Benzenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-fluoro-N-methyl- 254740-93-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(dimethylamino)carbonyl)methylamino)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-94-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(1,1-dimethylethyl)amino)carbonyl)methylamino)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-95-9P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]methyl-, ethyl ester 254740-96-0P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]methyl-, 2-methylpropyl ester 254740-97-1P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3,3-trimethyl- 254740-98-2P, 2-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254740-99-3P, 3-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254741-00-9P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254741-01-0P, 1H-Pyrrole-2-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,1-dimethyl- 254741-02-1P, 1,2,3-Thiadiazole-4-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254741-03-2P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,5-dimethyl- 254741-04-3P, 4-Isoxazolecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3,5-trimethyl- 254741-05-4P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,3-dimethyl- 254741-06-5P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N,5-dimethyl- 254741-07-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[4,5-dimethyl-3-isoxazolyl)amino)sulfonyl][1,1'-

biphenyl]-2-yl)methyl]-3-cyano-N-methyl- 254741-08-7P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-cyano-N-methyl- 254741-09-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-methoxy-N-methyl- 254741-10-1P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2-chloro-N-methyl- 254741-11-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-chloro-N-methyl- 254741-12-3P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-4-chloro-N-methyl- 254741-13-4P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-2,3-difluoro-N-methyl- 254741-14-5P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3,4-difluoro-N-methyl- 254741-15-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3,5-difluoro-N-methyl- 254741-16-7P, Benzamide, 4-acetyl-N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-N-methyl- 254741-17-8P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]-3-ethoxy-N-methyl- 254741-19-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(propylsulfonyl)amino]- 254741-20-3P, L-Valine, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-(1-oxopentyl)-, methyl ester 254741-22-5P, L-Valine, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-(1-oxopentyl)- 254741-24-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(4-oxo-2-propyl-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254741-26-9P, Butanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl)methyl]-N,3,3-trimethyl- 254741-27-0P, Pentanamide, N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254741-28-1P, Pentanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-30-5P, Pentanamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254741-31-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[[[(2,2,2-trifluoroethyl)amino]methyl]- 254741-32-7P, [1,1'-Biphenyl]-2-carboxylic acid, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]- 254741-33-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(trifluoromethyl)- 254741-34-9P, [1,1'-Biphenyl]-2-carboxylic acid, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-, methyl ester 254741-35-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(methoxymethyl)- 254741-36-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-fluoro- 254741-37-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254741-38-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)- 254741-39-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)- 254741-40-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-methyl- 254741-41-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254741-42-9P, Pentanamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-43-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[[2,2,2-trifluoroethyl)amino]methyl]- 254741-44-1P, Benzeneacetamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]- 254741-45-2P, Butanamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]-3,3-dimethyl- 254741-46-3P, [1,1'-Biphenyl]-2-sulfonamide, 2'-amino-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254741-48-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-nitro- 254741-50-9P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-52-1P, Cyclopropanecarboxamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-54-3P, Benzenepropanamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-56-5P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-58-7P, Hexanamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-60-1P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-62-3P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,4-dimethyl-, (2S)- 254741-64-5P, Cyclopropanecarboxamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-66-7P, Benzenepropanamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-68-9P, Benzeneacetamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-70-3P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254741-72-5P, Hexanamide, N-[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-74-7P, Pentanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254741-76-9P, Butanamide, 2-[[[2'-[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S)- 254741-78-1P, Cyclopropanecarboxamide,

N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-80-5P, Benzenepropanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-82-7P, Benzeneacetamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-85-0P, Butanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-3-methyl-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-87-2P, Hexanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-89-4P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)-254741-91-8P, Pentanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-1-[(ethylamino)carbonyl]-2-methylpropyl]-254741-93-0P, Pentanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-1-[(hexylamino)carbonyl]-2-methylpropyl]-254741-95-2P, Pentanamide, N-[[2-cyano-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-97-4P, Pentanamide, N-[[2-(cyanomethyl)-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-254741-99-6P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-254742-01-3P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-N,N-dimethyl-254742-03-5P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-N-methyl-254742-05-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(methoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254742-06-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]-2'-methyl-254742-07-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-methyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254742-08-0P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)-254742-09-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(hydroxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-254742-10-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl]oxy]methyl]-254742-11-5P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-fluoro[1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)-254742-12-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(phenoxymethyl)-254742-13-7P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(1H-pyrazol-1-yl)methyl][1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)-254742-14-8P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-254742-15-9P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)-254742-16-0P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-254742-17-1P, Butanamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)-254742-18-2P, Pentanamide, N-[[2-chloro-2'-[[[4,5-

dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-19-3P, Pentanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(trifluoromethyl)][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-20-6P, Cyclobutanecarboxamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-21-7P, 1H-Imidazole-5-carboxylic acid, 1-[[2-chloro-2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl]- 254742-22-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(methylsulfonyl)amino]- 254742-23-9P, Pentanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(4-methyl-1-piperazinyl)carbonyl]propyl]- 254742-24-0P, Pentanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-(1-piperidinylcarbonyl)propyl]- 254742-25-1P, Pentanamide, N-[(1S)-1-[[[(3,3-dimethylbutyl)amino]carbonyl]-2-methylpropyl]-N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254742-28-4P, Pentanamide, N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-1-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-methylpropyl]- 254742-29-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(1-methylethoxy)methyl]- 254742-31-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(propoxymethyl)- 254742-33-1P, 1H-Imidazole-5-carboxamide, 4-chloro-1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-propyl]- 254742-35-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-fluoro-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-36-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-oxo-1(2H)-pyridinyl)methyl]- 254742-37-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(1H-pyrazol-1-yl)methyl]- 254742-38-6P, 1H-Imidazole-5-carboxamide, 2-butyl-4-chloro-1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]- 254742-39-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[(2-methyl-4-quinolinyl)oxy]methyl]- 254742-41-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-43-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254742-45-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[(2-propyl-4-quinolinyl)oxy]methyl]- 254742-46-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(6,7-dihydro-2,4-dimethyl-7-oxopyrido[2,3-d]pyrimidin-8(5H)-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-47-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-49-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254742-51-3P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-N-methyl- 254742-53-5P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-, phenylmethyl ester 254742-54-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-, 2-phenylethyl ester 254742-56-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-, 2-(2-oxo-1-pyrrolidinyl)ethyl ester 254742-58-0P,

1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-, 3-(2-oxo-1-pyrrolidinyl)propyl ester 254742-60-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[2-ethyl-4-quinolinyl)oxy]methyl]- 254742-62-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-64-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254742-65-9P, 1H-Imidazole-5-carboxamide, 1-[[2-chloro-2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254742-66-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254742-67-1P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-N-methyl- 254742-68-2P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-N,N-dimethyl- 254742-69-3P, 3-Pyridinecarboxylic acid, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]propylamino]- 254742-70-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-71-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-72-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2,7-diethyl-5H-pyrazolo[1,5-b][1,2,4]triazol-5-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-73-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-butyl-6-[[[methyl(1'-methylethyl)amino]carbonyl]amino]-4-oxo-3(4H)-quinazolinyl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-75-1P, 3-Pyridinecarboxamide, 2-[[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]propylamino]-N-methyl- 254742-76-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254742-77-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[[[3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254742-78-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[[[3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-79-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(methoxymethyl)- 254742-80-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethyl-4-methyl- 254742-81-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-3(4H)-quinazolinyl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-82-0P, Pentanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[[[3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-83-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[[[4,4-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254742-84-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[[[3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254742-85-3P, Acetamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[[[2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl)methyl]methylamino]ethyl]- 254742-86-4P, [1,1'-Biphenyl]-2-acetic acid, 2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[[[2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-, ethyl ester 254742-87-5P, Pentanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[(propylamino)carbonyl]propyl]- 254742-88-6P, Pentanamide, N-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-[[[(tetrahydro-2-furanyl)methyl]amino]carbonyl]propyl]- 254742-89-7P

[1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)-4'-  
[[ (2-ethyl-4-quinolinyl)oxy]methyl]- 254742-91-1P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[ (2-ethyl-4-  
quinolinyl)oxy]methyl]-2'-(trifluoromethyl)- 254742-92-2P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)- 254742-93-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-methylpropoxy)methyl]-  
254742-94-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-  
[(ethylsulfonyl)amino]- 254742-95-5P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-  
dimethyl-3-isoxazolyl)-2'-[(2,2,2-trifluoroethoxy)methyl]- 254742-96-6P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-  
254742-97-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-  
2'-(ethoxymethyl)-4'-[[ (3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-  
254742-98-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-  
2'-(ethoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-  
cycloheptimidazolyl)methyl]- 254742-99-9P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(4,5-dimethyl-3-isoxazolyl)-2'-(3,3,3-trifluoropropyl)- 254743-00-5P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(3-fluoropropyl)-  
254743-01-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(1,1-difluoroethyl)-N-(4,5-  
dimethyl-3-isoxazolyl)- 254743-03-8P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-  
dimethyl-3-isoxazolyl)-2'-(2,2,2-trifluoroethyl)- 254743-05-0P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methylpropoxy)-  
254743-06-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-  
methoxyethoxy)- 254743-08-3P, [1,1'-Biphenyl]-2-sulfonamide,  
2'-butyl-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(4,5-dimethyl-3-isoxazolyl)- 254743-10-7P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(4,5-dimethyl-3-isoxazolyl)-2'-[(methoxymethylamino)methyl]-  
254743-12-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(2,2-difluoroethoxy)methyl]-N-  
(4,5-dimethyl-3-isoxazolyl)- 254743-15-2P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-  
(4,5-dimethyl-3-isoxazolyl)-2'-(2-fluoroethyl)- 254743-16-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-hydroxyethyl)-  
254743-17-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(3-  
methylbutyl)- 254743-18-5P, [1,1'-Biphenyl]-2-sulfonamide,  
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-  
dimethyl-3-isoxazolyl)-2'-(2-methylpropyl)- 254743-19-6P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(3,3-difluorobutyl)-4-oxo-1,3-  
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-  
(ethoxymethyl)- 254743-20-9P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(4,5-dimethyl-3-isoxazolyl)-4'-[[ (3-methoxy-2,6-dimethyl-4-  
pyridinyl)oxy]methyl]-2'-(3,3,3-trifluoropropyl)- 254743-22-1P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-  
en-3-yl)methyl]-2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-  
isoxazolyl)- 254743-24-3P, 1H-Imidazole-5-carboxamide,  
1-[[2'-[[ (4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-  
biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254743-25-4P,  
1H-Imidazole-5-carboxamide, 1-[[2'-[[ (4,5-dimethyl-3-  
isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-  
ethyl-N-methyl-2-propyl- 254743-26-5P, 1H-Imidazole-5-carboxamide,



1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254743-27-6P,  
1H-Imidazole-5-carboxamide, 1-[[2'-[[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254743-28-7P 254743-29-8P 254743-30-1P  
254743-31-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl- 254743-32-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)- 254743-33-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)- 254743-34-5P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-ethyl-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-35-6P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-36-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-37-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-38-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-39-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-40-3P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-41-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-42-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-43-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-44-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-45-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-46-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-ethyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-47-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-48-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-49-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-50-5P 254743-51-6P 254743-53-8P 254743-56-1P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-57-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-58-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(tetrahydro-2-furanyl)- 254743-59-4P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-61-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-



254743-62-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'--(tetrahydro-2-furanyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-63-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)- 254743-64-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)- 254743-65-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(tetrahydro-2-furanyl)- 254743-66-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]- 254743-67-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]- 254743-68-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]-2'-(tetrahydro-2-furanyl)- 254743-69-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-70-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-71-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(tetrahydro-2-furanyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-72-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-2'-(3,3,3-trifluoropropyl)- 254743-73-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-2'-(3,3,3-trifluoropropyl)- 254743-74-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]-2'-propyl- 254743-75-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]-2'-propyl- 254743-76-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-77-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-propyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-78-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]-

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254743-79-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl]oxy]methyl]- 254743-80-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-81-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-82-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(2,2-difluorobutyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl- 254743-83-4P 254743-84-5P 254743-85-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[[4-oxo-2-(4,4,4-trifluorobutyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254743-86-7P 254743-87-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[4-oxo-2-(4,4,4-trifluorobutyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-2'-propyl- 254743-88-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[[4-oxo-2-(3,3,3-trifluoropropyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254743-89-0P

254743-90-3P 254743-91-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[4-oxo-2-(3,3,3-trifluoropropyl)-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-propyl- 254743-92-5P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy)methyl]- 254743-93-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[3-methoxy-2,6-dimethyl-4-pyridinyl)oxy)methyl]- 254743-94-7P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-95-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-96-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1,1,3,3,3-pentafluoropropyl)- 254743-97-0P 254743-98-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254743-99-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-00-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-01-9P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-02-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-03-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-04-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-05-3P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-06-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-07-5P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-08-6P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-09-7P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-N-methyl-2-propyl- 254744-10-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-11-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-12-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254744-13-3P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl-

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 56-12-2, 4-Aminobutyric acid, reactions 75-03-6, Iodoethane 78-09-1, Tetraethyl orthocarbonate 79-03-8, Propionyl chloride 79-44-7, Dimethylcarbamyl chloride 95-89-6, 2-Chloro-3,6-dimethylpyrazine

109-81-9, N-Methylethylenediamine 124-40-3, Dimethylamine, reactions  
 127-08-2, Potassium acetate 541-41-3, Ethyl chloroformate 543-27-1,  
 Isobutyl chloroformate 589-15-1, 4-Bromobenzyl bromide 627-03-2,  
 Ethoxyacetic acid 638-29-9, Valeryl chloride 676-58-4, Methylmagnesium  
 chloride 680-15-9, Acetic acid, difluoro(fluorosulfonyl)-, methyl ester  
 767-00-0, 4-Cyanophenol 865-33-8, Potassium methoxide 873-75-6,  
 4-Bromobenzyl alcohol 1117-97-1, N-Methoxy-N-methylamine 1122-91-4,  
 4-Bromobenzaldehyde 1450-75-5, Ethanone, 1-(5-bromo-2-hydroxyphenyl)-  
 1530-32-1, Ethyltriphenylphosphonium bromide 1609-86-5, tert-Butyl  
 isocyanate 2835-98-5, Phenol, 2-amino-5-methyl- 2905-25-1,  
 2-Bromobenzenesulfonyl chloride 3959-07-7, 4-Bromobenzylamine  
 4858-85-9, 2,3-Dichloropyrazine 5326-34-1, 4-Bromo-3-nitrotoluene  
 6228-47-3, Propyltriphenylphosphonium bromide 6482-24-2,  
 1-Bromo-2-methoxyethane 13734-41-3, L-Valine, N-[(1,1-  
 dimethylethoxy)carbonyl]- 14508-49-7, 2-Chloropyrazine 14678-02-5,  
 5-Amino-3-methylisoxazole 22059-22-9, Acetamide oxime 22884-29-3,  
 Isobutyltriphenylphosphonium bromide 28466-21-9, 4-Amino-1,3,5-  
 trimethylpyrazole 29006-02-8, Butanoic acid, 4-methoxy- 33670-32-5,  
 Methoxymethyltriphenylphosphonium bromide 34328-47-7, Benzaldehyde,  
 4-bromo-3-(trifluoromethyl)- 34841-06-0, 3-Bromo-4-methoxybenzaldehyde  
 40155-28-0, 2-Chloro-3-methoxypyrazine 41963-20-6, 4-Bromo-3-  
 methylbenzonitrile 53553-14-3, Methyl 2-chloro-3-nitrobenzoate  
 53596-60-4, Benzoic acid, 4-hydroxy-3-(2-propenyl)-, methyl ester  
 60421-23-0, Cyclopentanecarboxylic acid, 1-amino-, methyl ester,  
 hydrochloride 74410-26-7, Butanamide, 2-amino-N,3-dimethyl-,  
 monohydrochloride, (2S)- 76513-69-4, 2-(Trimethylsilyl)ethoxymethyl  
 chloride 78775-11-8, Benzaldehyde, 4-bromo-3-methyl- 87199-17-5,  
 4-Formylphenylboronic acid 89464-87-9, 2-Amino-3-methoxy-5-  
 methylpyrazine 98946-18-0, tert-Butyl 2,2,2-trichloroacetimidate  
 109072-25-5, 4(1H)-Quinolinone, 2-ethyl- 120077-69-2, Benzaldehyde,  
 4-bromo-3-chloro- 124750-49-8, 1H-Imidazole-4-carboxaldehyde,  
 5-chloro-2-propyl- 125110-82-9, 4,4-Difluoropentanoic acid  
 133059-43-5, Benzaldehyde, 4-bromo-3-fluoro- 133240-06-9,  
 1H-Imidazo[4,5-b]pyridine, 2-ethyl-5,7-dimethyl- 138402-05-8,  
 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-butyl- 148547-19-7, Methyl  
 4-bromo-3-methylbenzoate 150691-04-6, Boronic acid, [2-[[[(1,1-  
 dimethylethyl)amino]sulfonyl]phenyl]- 151257-01-1, 1,3-  
 Diazaspiro[4.4]non-1-en-4-one, 2-butyl-, monohydrochloride 153039-15-7,  
 Butanoic acid, 4-amino-2,2-dimethyl-, hydrochloride 160313-50-8,  
 Benzonitrile, 4-bromo-3-(1,3-dioxolan-2-yl)- 162647-41-8, 4-Pyridinol,  
 3-methoxy-2,6-dimethyl- 167985-34-4, 1H-Imidazole-4-carboxylic acid,  
 5-ethyl-2-propyl-, ethyl ester 176961-13-0, Boronic acid,  
 [2-[[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]ph  
 enyl]- 195436-86-3, Benzenesulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-  
 [(2-methoxyethoxy)methyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-  
 254746-77-5, Boronic acid, [2-[[[(4,5-dimethyl-3-isoxazolyl)[(2-  
 methoxyethoxy)methyl]amino]sulfonyl]phenyl]- 254746-78-6, Butanoic acid,  
 4-amino-2,2-dimethyl-, ethyl ester, hydrochloride 254746-79-7, Boronic  
 acid, [2-[[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]meth  
 yl]amino]sulfonyl]phenyl]- 254746-80-0, [1,1'-Biphenyl]-2-sulfonamide,  
 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-(ethoxymethyl)-N-[(2-  
 methoxyethoxy)methyl]- 254746-81-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as  
 dual angiotensin II and endothelin receptor antagonists)

IT 14847-51-9P, Phenol, 2-bromo-5-methyl- 79047-47-5P, 1H-Imidazole-4-  
 methanol, 5-chloro-2-propyl- 89003-95-2P, Benzonitrile,  
 4-bromo-3-formyl- 123652-98-2P, Benzene, 2-bromo-4-(dimethoxymethyl)-1-  
 methoxy- 142031-67-2P, Benzoic acid, 4-bromo-3-(bromomethyl)-, methyl  
 ester 160313-48-4P, Benzenemethanol, 4-bromo-3-(1,3-dioxolan-2-yl)-  
 176961-30-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-  
 dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]- 189762-06-9P,  
 [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-

[(2-methoxyethoxy)methyl]- 189762-08-1P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl- 190197-86-5P, Benzonitrile,  
4-bromo-3-(bromomethyl)- 254744-14-4P, Benzonitrile,  
3-[(acetyloxy)methyl]-4-bromo- 254744-15-5P, Benzaldehyde,  
4-bromo-3-(hydroxymethyl)- 254744-16-6P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(hydroxymethyl)-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-17-7P, Benzonitrile,  
4-bromo-3-(methoxymethyl)- 254744-18-8P, Benzaldehyde,  
4-bromo-3-(methoxymethyl)- 254744-19-9P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-  
(methoxymethyl)- 254744-20-2P, [1,1'-Biphenyl]-2-sulfonamide,  
N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-  
methoxyethoxy)methyl]-2'-(methoxymethyl)- 254744-21-3P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-  
isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(methoxymethyl)-  
254744-22-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-  
isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-23-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
2'-formyl-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-24-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-  
isoxazolyl)-4'-formyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-25-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
4'-formyl-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-26-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-methyl- 254744-27-9P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro-4'-  
formyl-N-[(2-methoxyethoxy)methyl]- 254744-28-0P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-  
[[[(methylsulfonyl)oxy]methyl]-2'-(trifluoromethyl)-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-29-1P, [1,1'-Biphenyl]-2-  
sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-  
[[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-30-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-  
dimethyl-5-isoxazolyl)-2'-fluoro-N-[(2-methoxyethoxy)methyl]-  
254744-31-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
4'-(hydroxymethyl)-2'-[[[(methylsulfonyl)oxy]methyl]-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-32-6P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-  
methyl-4'-[[[(methylsulfonyl)oxy]methyl]- 254744-33-7P,  
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-  
(hydroxymethyl)-4'-[[[(methylsulfonyl)oxy]methyl]-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-34-8P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-methyl-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-35-9P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[[2-  
[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-36-0P, [1,1'-Biphenyl]-2-  
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-  
[[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-37-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
4'-formyl-2'-(methoxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-  
254744-38-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-  
2'-formyl-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-39-3P  
254744-40-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-  
4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-41-7P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(4,5-dimethyl-3-  
isoxazolyl)-N-[(2-methoxyethoxy)methyl]- 254744-42-8P 254744-43-9P,  
[1,1'-Biphenyl]-2-sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-2'-  
formyl-N-[(2-methoxyethoxy)methyl]- 254744-44-0P, [1,1'-Biphenyl]-2-  
sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-  
methoxyethoxy)methyl]-2'-[(methylamino)methyl]- 254744-45-1P, Carbamic  
acid, [[4-cyano-2'-[(3,4-dimethyl-5-isoxazolyl)(2-  
methoxyethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-2-yl)methylmethyl-,  
1,1-dimethylethyl ester 254744-46-2P, Carbamic acid,

[[2'-[[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]-4-formyl[1,1'-biphenyl]-2-yl)methyl]methyl-, 1,1-dimethylethyl ester 254744-47-3P, Carbamic acid, [[4-(bromomethyl)-2'-[[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-2-yl)methyl]methyl-, 1,1-dimethylethyl ester 254744-48-4P 254744-49-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-N-[(2-methoxyethoxy)methyl]- 254744-50-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-4'-formyl-N-[(2-methoxyethoxy)methyl]- 254744-51-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-N-[(2-methoxyethoxy)methyl]- 254744-52-0P 254744-53-1P, Benzaldehyde, 4-bromo-3-(1,3-dioxolan-2-yl)- 254744-54-2P, 1,3-Dioxolane, 2-[2-bromo-5-(bromomethyl)phenyl]- 254744-55-3P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(1,3-dioxolan-2-yl)phenyl]methyl]-2-butyl-, 254744-56-4P 254744-58-6P 254744-60-0P 254744-63-3P 254744-65-5P 254744-68-8P 254744-70-2P 254744-73-5P, 1,2,4-Oxadiazole-5-methanamine, 3-methyl-.alpha.-(1-methylethyl)-, (.alpha.S)- 254744-78-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[[(1S)-2-methyl-1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]amino]methyl]- 254744-81-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-84-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]- 254744-86-0P, Cyclopentanecarboxylic acid, 1-[(3-methoxy-1-oxopropyl)amino]-, methyl ester 254744-87-1P, Cyclopentanecarboxylic acid, 1-[(3-methoxy-1-oxopropyl)amino]- 254744-90-6P, Cyclopentanecarboxamide, 1-[(3-methoxy-1-oxopropyl)amino]- 254744-91-7P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(2-methoxyethyl)- 254744-95-1P, Cyclopentanecarboxylic acid, 1-[(ethoxyacetyl)amino]-, methyl ester 254744-98-4P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(ethoxymethyl)- 254745-00-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl-N-[(2-methoxyethoxy)methyl]-4'-[(methylsulfonyl)oxy]- 254745-03-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-formyl-N-[(2-methoxyethoxy)methyl]- 254745-06-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]-2'-[(2-oxo-1-pyrrolidinyl)methyl]- 254745-08-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254745-12-5P, Benzenesulfonamide, 2-bromo-N-(3-methyl-5-isoxazolyl)- 254745-14-7P, Benzenesulfonamide, 2-bromo-N-(3-methyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-19-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-formyl-N-(3-methyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-23-8P, Butanamide, N,3-dimethyl-2-[[[2'-[[[(3-methyl-5-isoxazolyl)[(2-[(trimethylsilyl)oxy]ethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]amino]-, (2S)- 254745-28-3P, Pentanamide, N-[[2'-[[[(3-methyl-5-isoxazolyl)[(2-[(trimethylsilyl)oxy]ethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl)methyl]-N-[(1S)-2-methyl-1-(methylamino)carbonyl]propyl]- 254745-31-8P, Benzonitrile, 4-bromo-3-(1-propenyl)- 254745-36-3P, Benzonitrile, 4-bromo-3-propyl- 254745-39-6P, Benzaldehyde, 4-bromo-3-propyl- 254745-42-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-propyl- 254745-43-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-propyl- 254745-45-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-4'-[[[(methylsulfonyl)oxy]methyl]-2'-propyl- 254745-46-5P 254745-48-7P, Benzoic acid, 2-[[[(4-bromophenyl)methyl]amino]-3-nitro-, methyl ester 254745-49-8P, Benzoic acid, 2-[[[2'-[[[(3,4-dimethyl-5-isoxazolyl)[(2-

[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]amino]-3-nitro-, methyl ester 254745-50-1P, Benzoic acid, 3-amino-2-[[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]amino]-, methyl ester 254745-51-2P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-, methyl ester 254745-52-3P, Benzenemethanamine, 4-bromo-3-(1,3-dioxolan-2-yl)- 254745-53-4P, Benzoic acid, 2-[[[4-bromo-3-(1,3-dioxolan-2-yl)phenyl)methyl]amino]-3-nitro-, methyl ester 254745-54-5P, Benzoic acid, 2-[[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl]-2-formyl[1,1'-biphenyl]-4-yl)methyl]amino]-3-nitro-, methyl ester 254745-55-6P, Benzoic acid, 2-[[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]amino]-3-nitro-, methyl ester 254745-57-8P, Benzoic acid, 3-amino-2-[[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]amino]-, methyl ester 254745-58-9P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl)methyl]-2-ethoxy-, methyl ester 254745-60-3P, Quinoline, 4-[(4-bromophenyl)methoxy]-2-ethyl- 254745-61-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(1,1-dimethylethyl)-4'-[[2-ethyl-4-quinolinyl)oxy)methyl]- 254745-62-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-ethyl-4-quinolinyl)oxy)methyl]- 254745-64-7P, [1,1'-Biphenyl]-2-sulfonic acid, 4'-[[2-ethyl-4-quinolinyl)oxy)methyl]- 254745-66-9P, Ethanone, 1-(5-chloro-2-propyl-1H-imidazol-4-yl)- 254745-68-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy)methyl]- 254745-70-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(4-chloro-5-formyl-2-propyl-1H-imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy)methyl]- 254745-72-7P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-[(trimethylsilyl)oxy]ethoxy)methyl]amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-propyl- 254745-73-8P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-2-propyl- 254745-76-1P, 1H-Imidazole-5-carboxylic acid, 1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)][2-methoxyethoxy)methyl]amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl-, ethyl ester 254745-77-2P, 1H-Imidazole-5-carboxylic acid, 1-[[2'-[[[3,4-dimethyl-5-isoxazolyl)amino)sulfonyl][1,1'-biphenyl]-4-yl)methyl]-4-ethyl-2-propyl- 254745-78-3P 254745-79-4P 254745-80-7P 254745-81-8P 254745-82-9P, Benzenesulfonamide, 2-bromo-N-(3-methoxy-5-methylpyrazinyl)- 254745-83-0P, Benzenesulfonamide, 2-bromo-N-(3-methoxy-5-methylpyrazinyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy)methyl]- 254745-84-1P 254745-85-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-formyl-N-(3-methoxy-5-methylpyrazinyl)- 254745-86-3P, Benzenesulfonamide, 2-bromo-N-[[2-methoxyethoxy)methyl]-N-(3-methyl-5-isoxazolyl)- 254745-87-4P, Boronic acid, [2-[[[2-methoxyethoxy)methyl](3-methyl-5-isoxazolyl)amino)sulfonyl]phenyl]- 254745-88-5P 254745-89-6P 254745-90-9P 254745-91-0P, Benzene, 4-(dimethoxymethyl)-1-methoxy-2-(3,3,3-trifluoropropyl)- 254745-92-1P, Benzaldehyde, 4-methoxy-3-(3,3,3-trifluoropropyl)- 254745-93-2P, Benzaldehyde, 4-hydroxy-3-(3,3,3-trifluoropropyl)- 254745-94-3P, Methanesulfonic acid, trifluoro-, 4-formyl-2-(3,3,3-trifluoropropyl)phenyl ester 254745-95-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy)methyl]- 254745-96-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy)methyl]- 254745-97-6P

254745-98-7P, Benzoic acid, 3-(2-propenyl)-4-[[trifluoromethyl)sulfonyl]oxy]-, methyl ester 254745-99-8P, Benzoic acid, 3-(3-hydroxypropyl)-4-[[trifluoromethyl)sulfonyl]oxy]-, methyl ester 254746-00-4P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[3,4-dimethyl-5-isoxazolyl][2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(3-hydroxypropyl)-, methyl ester 254746-01-5P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[3,4-dimethyl-5-isoxazolyl][2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(3-fluoropropyl)-, methyl ester 254746-03-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-04-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-4'-[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-06-0P 254746-07-1P, Methanesulfonic acid, trifluoro-, 2-acetyl-4-bromophenyl ester 254746-08-2P, Methanesulfonic acid, trifluoro-, 4-bromo-2-(1,1-difluoroethyl)phenyl ester 254746-09-3P, Methanesulfonic acid, trifluoro-, 2-(1,1-difluoroethyl)-4-formylphenyl ester 254746-10-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-11-7P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-12-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-13-9P 254746-14-0P, Benzoic acid, 4-bromo-3-(2,2,2-trifluoroethyl)-, methyl ester 254746-15-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[3,4-dimethyl-5-isoxazolyl][2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2,2,2-trifluoroethyl)-, methyl ester 254746-16-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-(2,2,2-trifluoroethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-18-4P 254746-19-5P, Benzene, 1-bromo-4-methyl-2-(2-methylpropoxy)-254746-20-8P, Benzene, 1-bromo-4-(bromomethyl)-2-(2-methylpropoxy)-254746-21-9P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(2-methylpropoxy)phenyl]methyl]-2-butyl-254746-22-0P 254746-23-1P, Benzene, 1-bromo-2-(2-methoxyethoxy)-4-methyl-254746-24-2P, Benzene, 1-bromo-4-(bromomethyl)-2-(2-methoxyethoxy)-254746-25-3P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(2-methoxyethoxy)phenyl]methyl]-2-butyl-254746-26-4P 254746-27-5P, Benzonitrile, 4-bromo-3-(1-butenyl)-254746-28-6P, Benzonitrile, 4-bromo-3-butyl-254746-29-7P, Benzaldehyde, 4-bromo-3-butyl-254746-30-0P, [1,1'-Biphenyl]-2-sulfonamide, 2'-butyl-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-31-1P, [1,1'-Biphenyl]-2-sulfonamide, 2'-butyl-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-32-2P 254746-33-3P, Boronic acid, [2-[(3-methyl-5-isoxazolyl)[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]phenyl]-254746-34-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-formyl-N-(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-35-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(hydroxymethyl)-N-(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-254746-36-6P 254746-37-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-[(methoxymethylamino)methyl]-254746-38-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-[(methoxymethylamino)methyl]-254746-39-9P 254746-40-2P, Benzoic acid, 4-bromo-3-(hydroxymethyl)-, methyl ester 254746-41-3P, Benzoic acid, 3-[(acetyloxy)methyl]-4-bromo-, methyl ester 254746-42-4P, Benzoic acid, 4-bromo-3-[[tetrahydro-2H-pyran-2-yl]oxy]methyl]-, methyl ester 254746-43-5P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[3,4-dimethyl-5-isoxazolyl][2-[(trimethylsilyl)oxy]ethoxy]meth



yl]amino]sulfonyl]-2-[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, methyl ester 254746-44-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-N-[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-45-7P 254746-46-8P 254746-47-9P 254746-48-0P, Benzoic acid, 3-(2-hydroxyethyl)-4-[(trifluoromethyl)sulfonyl]oxy]-, methyl ester 254746-49-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[(3,4-dimethyl-5-isoxazolyl)[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2-hydroxyethyl)-, methyl ester 254746-50-4P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[(3,4-dimethyl-5-isoxazolyl)[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2-fluoroethyl)-, methyl ester 254746-51-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-fluoroethyl)-4'-(hydroxymethyl)-N-[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-52-6P 254746-53-7P

[1,1'-Biphenyl]-4-carboxylic acid, 2'-[(3,4-dimethyl-5-isoxazolyl)[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-, methyl ester 254746-54-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-N-[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-55-9P, Benzonitrile, 4-bromo-3-(3-methyl-1-butenyl)- 254746-56-0P, Benzonitrile, 4-bromo-3-(3-methylbutyl)- 254746-57-1P, Benzaldehyde, 4-bromo-3-(3-methylbutyl)- 254746-58-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-(3-methylbutyl)- 254746-59-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(3-methylbutyl)- 254746-60-6P, Benzonitrile, 4-[(2-methyl-2-propenyl)oxy]- 254746-61-7P, Benzonitrile, 4-hydroxy-3-(2-methyl-2-propenyl)- 254746-62-8P, Benzonitrile, 4-hydroxy-3-(2-methylpropyl)- 254746-63-9P, Benzaldehyde, 4-hydroxy-3-(2-methylpropyl)- 254746-64-0P, Methanesulfonic acid, trifluoro-, 4-formyl-2-(2-methylpropyl)phenyl ester 254746-65-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-66-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-67-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-68-4P 254746-69-5P, Cyclopentanecarboxylic acid, 1-[(3,3-difluoro-1-oxobutyl)amino]-, methyl ester 254746-70-8P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(3,3-difluorobutyl)- 254746-71-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-72-0P, Benzoic acid, 4-bromo-3-[(1,1-dimethylethoxy)methyl]-, methyl ester 254746-73-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2-[(1,1-dimethylethoxy)methyl]-2'-[(3,4-dimethyl-5-isoxazolyl)[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-, methyl ester 254746-74-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-75-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-76-4P 254746-82-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 50-78-2, Aspirin 52-01-7, Spironolactone 10238-21-8, Glyburide 51384-51-1, Metoprolol 55142-85-3, Ticlopidine 72956-09-3, Carvedilol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 107724-20-9, Eplerenone 113665-84-2, Clopidogrel 134523-00-5, Atorvastatin 147098-20-2, Zidovudine 147526-32-7, NK 104 150322-43-3, Cs-747

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)



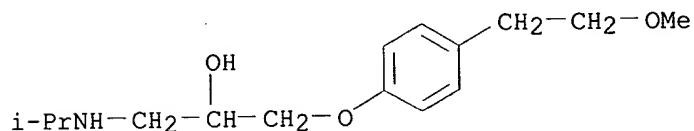
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 51384-51-1, Metoprolol 107724-20-9,  
Eplerenone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

RN 51384-51-1 HCAPLUS

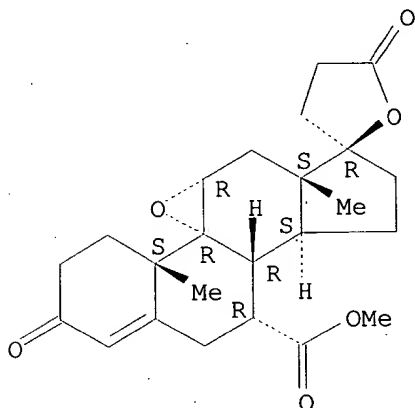
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)  
(CA INDEX NAME)



RN 107724-20-9 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
.gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:107159 HCAPLUS

DN 136:172753

TI Epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
combination therapy for treatment of congestive heart failure

IN Alexander, John C.; Schuh, Joseph R.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 190 pp.  
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K045-06  
ICS A61K031-58; A61P009-00; A61K031-58; A61K031-135; A61K045-06;  
A61K031-58

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 2

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002009760 A2 20020207 WO 2001-US23670 20010727 <--  
 WO 2002009760 A3 20030123

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002123485 A1 20020905 US 2001-917403 20010727 <--  
 EP 1303306 A2 20030423 EP 2001-957290 20010727 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-221365P P 20000727 <--  
 WO 2001-US23670 W 20010727 <--

AB A combination therapy comprising a therapeutically-effective amt. of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amt. of a beta-adrenergic antagonist is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred beta-adrenergic antagonists are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9.alpha., 11.alpha.-substituted epoxy moiety. A preferred combination therapy includes the beta-adrenergic antagonist **metoprolol** succinate and the aldosterone receptor antagonist **epoxymexrenone**. Crystal forms of **epplerenone** were prepd. as well as the Me Et ketone solvate.

ST epoxy steroid aldosterone antagonist beta adrenergic antagonist;  
 congestive heart failure treatment compn

IT Cardiovascular agents  
 Crystal morphology  
 Crystallization  
 Human  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Mineralocorticoid receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Steroids, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Heart, disease  
 (failure; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

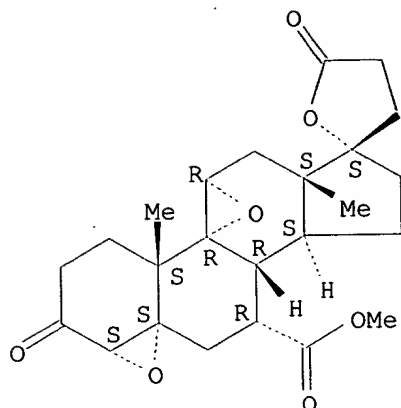
IT Adrenoceptor antagonists  
 (.beta.-; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT 170684-14-7, UK 1745  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (UK 1745; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT 52-39-1, Aldosterone  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of

- congestive heart failure)
- IT **395665-44-8P 395665-46-0P**  
 RL: BYP (Byproduct); PREP (Preparation)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)
- IT **344449-96-3**  
 RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic  
 use); BIOL (Biological study); FORM (Formation, nonpreparative); USES  
 (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)
- IT **107724-20-9, Eplerenone**  
 RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical  
 process); PRP (Properties); PYP (Physical process); THU (Therapeutic use);  
 BIOL (Biological study); PROC (Process); USES (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)
- IT 52-01-7, Spironolactone 525-66-6, Propranolol 3930-20-9, Sotalol  
 6452-71-7, Oxprenolol 7413-36-7, Nifenalol 13523-86-9, Pindolol  
 13655-52-2, Alprenolol 22664-55-7, Metipranolol 23694-81-7, Mepindolol  
 26839-75-8, Timolol 29122-68-7, Atenolol 34915-68-9, Bunitrolol  
 36894-69-6, Labetalol 37517-30-9, Acebutolol 38363-40-5, Penbutolol  
 39552-01-7, Befunolol 39563-28-5, Cloranolol 42200-33-9, Nadolol  
 47141-42-4, Levobunolol **51384-51-1, Metoprolol**  
 51781-06-7, Carteolol 56980-93-9, Celiprolol 57460-41-0, Talinolol  
 57775-29-8, Carazolol 58409-59-9, Bucumolol 58930-32-8, Butofilolol  
 59170-23-9, Bevantolol 60607-68-3, Indenolol 62658-63-3, Bopindolol  
 63659-18-7, Betaxolol 66722-44-9, Bisoprolol 66848-46-2, Viskenit  
 68377-92-4, Arotinolol 71119-11-4, Bucindolol 72956-09-3, Carvedilol  
 77164-20-6, Levomoprolol 81147-92-4, Esmolol 81447-80-5, Diprafenone  
 81486-22-8, Nipradilol 81801-12-9, Xamoterol 83688-84-0, Tertatolol  
 85136-71-6, Tilisolol 85320-68-9, Amosulalol 93379-54-5, S-Atenolol  
 98418-47-4, Toprol xl 102203-23-6, Acc 9369 114856-47-2, TZC-5665  
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 132017-03-9, SR 58894A 133242-30-5, Landiolol 153192-22-4, YM-430  
 153601-03-7, Capsinolol 165337-66-6, LM-2616 174689-39-5, SR-59230A  
 188564-74-1, Fr-172516 207922-70-1 264134-39-6, SB-226552  
**395665-48-2 395665-50-6 395665-52-8**  
**395665-54-0 395665-56-2 395665-58-4**  
**395665-60-8 395665-62-0 395665-64-2**  
**395665-66-4 395665-68-6** 396654-09-4 396712-03-1, AMO  
 140 396712-06-4, ISV 208 396712-07-5, PharmaProjects 5279  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)
- IT **395665-44-8P 395665-46-0P**  
 RL: BYP (Byproduct); PREP (Preparation)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)
- RN 395665-44-8 HCAPLUS
- CN Pregnane-7,21-dicarboxylic acid, 4,5:9,11-diepoxy-17-hydroxy-3-oxo-,  
 .gamma.-lactone, methyl ester, (4.alpha.,5.alpha.,7.alpha.,11.alpha.)-  
 (9CI) (CA INDEX NAME)

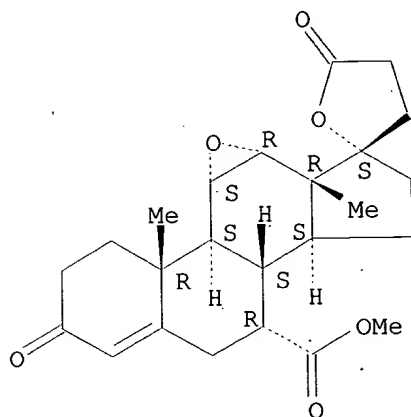
Absolute stereochemistry.



RN 395665-46-0 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 11,12-epoxy-17-hydroxy-3-oxo-,  
.gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,12.alpha.)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



IT 344449-96-3

RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)  
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 344449-96-3 HCAPLUS

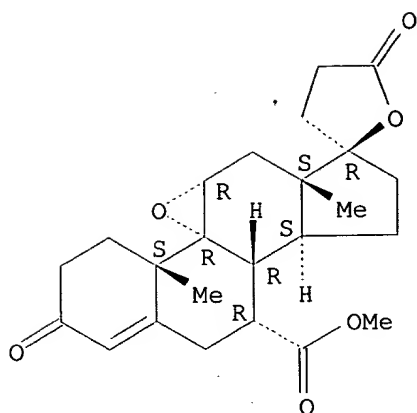
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
.gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)-, compd.  
with 2-butanone (9CI) (CA INDEX NAME)

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CRN 107724-20-9

CMF C24 H30 O6

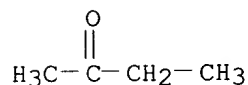
Absolute stereochemistry.



CM 2

CRN 78-93-3

CMF C4 H8 O



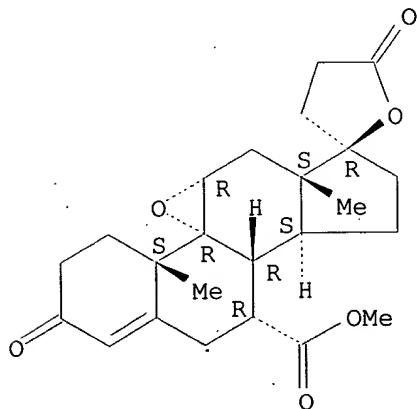
IT 107724-20-9, Eplerenone

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 107724-20-9 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone; methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 51384-51-1, Metoprolol 395665-48-2  
 395665-50-6 395665-52-8 395665-54-0  
 395665-56-2 395665-58-4 395665-60-8

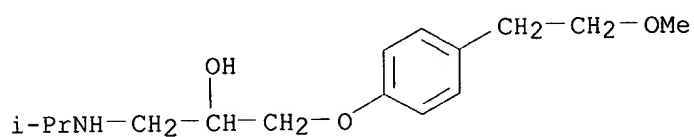
395665-62-0 395665-64-2 395665-66-4

395665-68-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist  
 combination therapy for treatment of congestive heart failure)

RN 51384-51-1 HCAPLUS

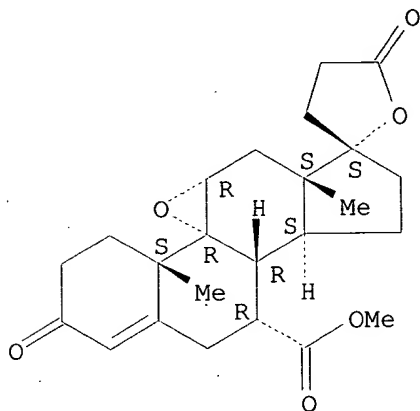
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)  
 (CA INDEX NAME)



RN 395665-48-2 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
 .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX  
 NAME)

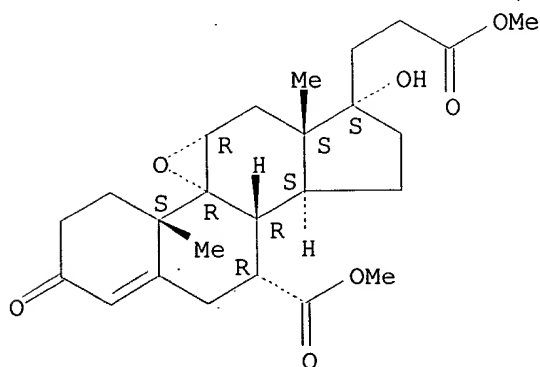
Absolute stereochemistry.



RN 395665-50-6 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl  
 ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

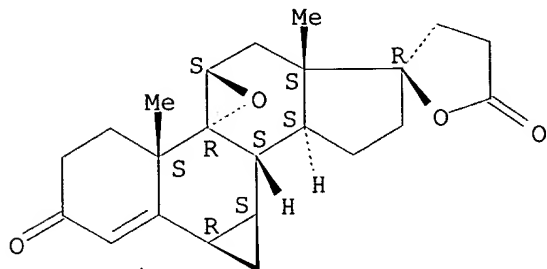
Absolute stereochemistry.



RN 395665-52-8 HCAPLUS

CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid,  
9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone,  
(6.alpha.,7.alpha.,11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)

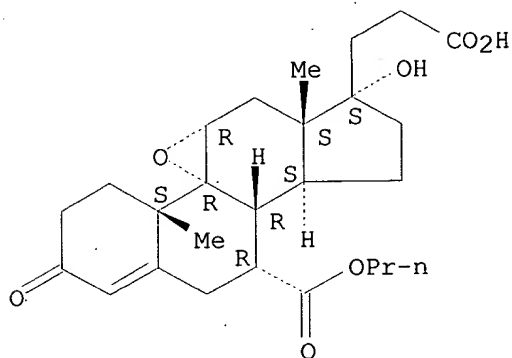
Absolute stereochemistry.



RN 395665-54-0 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-propyl  
ester, monopotassium salt, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

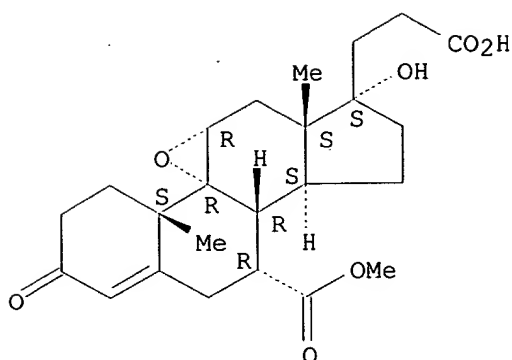


● K

RN 395665-56-2 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl  
ester, monopotassium salt, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

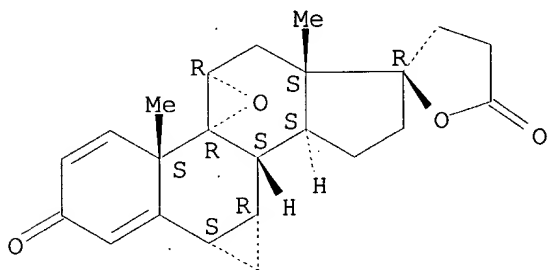
Absolute stereochemistry.



● K

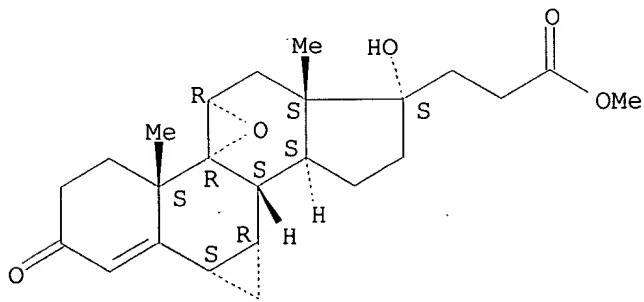
RN 395665-58-4 HCAPLUS  
 CN 3'H-Cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid,  
 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone,  
 (6.beta.,7.beta.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-60-8 HCAPLUS  
 CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid,  
 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester,  
 (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

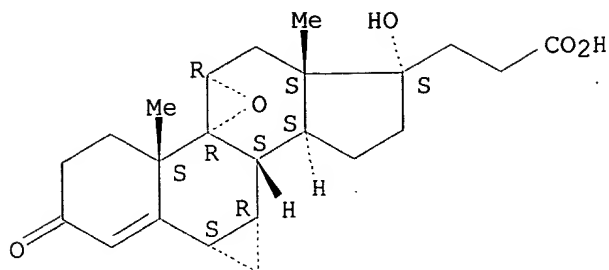
Absolute stereochemistry.



RN 395665-62-0 HCAPLUS  
 CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid,  
 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt,  
 (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)



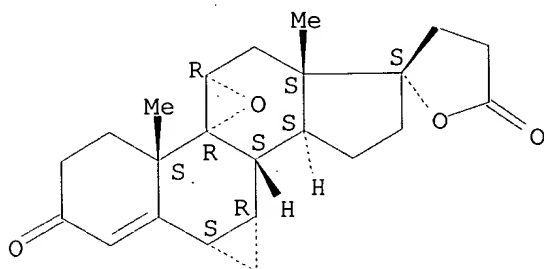
Absolute stereochemistry.



● K

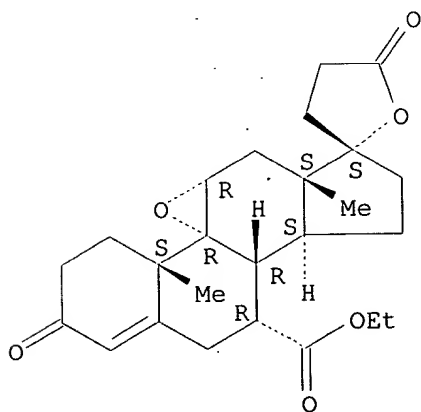
RN 395665-64-2 HCAPLUS  
 CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid,  
 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone,  
 (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-66-4 HCAPLUS  
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
 .gamma.-lactone, ethyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

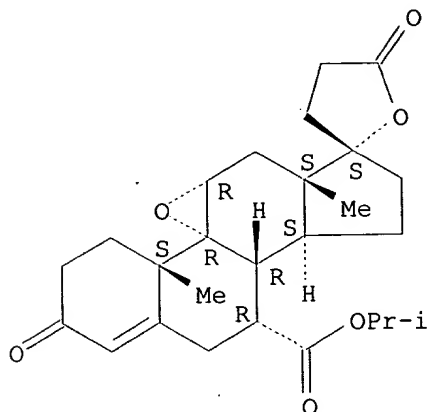
Absolute stereochemistry.



RN 395665-68-6 HCAPLUS  
 CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,

.gamma.-lactone, 1-methylethyl ester, (7.alpha.,11.alpha.)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:259979 HCAPLUS

DN 132:288794

TI Sympathetic nervous system activity-reducing agents for treatment of  
disease- or age-related weight loss and for enhancement of exercise  
performance

IN Anker, Stefan Dietmar; Coats, Andrew Justin Stewart

PA Imperial College Innovations Limited, UK

SO PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 1-12 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021509	A2	20000420	WO 1999-GB3302	19991015
	WO 2000021509	A3	20001109		
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1121111	A2	20010808	EP 1999-947762	19991015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002527378	T2	20020827	JP 2000-575485	19991015
PRAI	GB 1998-22458	A	19981015		
	GB 1998-22459	A	19981015		
	GB 1999-17181	A	19990723		
	WO 1999-GB3302	W	19991015		

AB A method of treating wt. loss due to underlying disease in a patient, the  
method comprising administering to the patient an effective amt. of an  
agent which reduces sympathetic nervous system activity. A method of  
treating wt. loss due to underlying disease in a patient, the method  
comprising administering to the patient an effective amt. of any one or  
more of the following: a compd. which inhibits the effect of aldosterone  
such as an aldosterone antagonist; a chymase inhibitor; a cathepsin B  
inhibitor; a .beta. receptor blocker; an imidazoline receptor antagonist;  
a centrally acting .alpha. receptor antagonist; a peripherally acting  
.alpha. receptor antagonist; a ganglion blocking agent; a drug that has an

effect on cardiovascular reflexes and thereby reduces SNS activity such as an opiate; scopolamine; an endothelin receptor antagonist; and a xanthine oxidase inhibitor. The methods are particularly useful in treating cardiac cachexia. The sympathetic nervous system activity-reducing agents may also be used to treat wt. loss due to aging and to enhance exercise performance.

ST sympathetic agent disease related wt loss; age related wt loss sympathetic agent; exercise performance cardiac cachexia sympathetic agent

IT Anabolic agents

(anabolic growth factors; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Angiotensin receptor antagonists

(angiotensin II; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Endothelin receptors

Imidazoline receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Reflex

(cardiovascular; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Lung, disease

(chronic obstructive; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Infection

(chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Muscle

(elec. stimulation of; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epoxysuccinyl; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Heart, disease

Kidney, disease

(failure, chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Nervous system agents

(ganglionic blocking agents; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Body weight

(loss; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT AIDS (disease)

Aging, animal

Cachexia

Cirrhosis

Disease, animal

Emphysema

Exercise

Heart, disease

Hypertension

Malnutrition

Neoplasm

Nervous system agents

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Opioids

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Nervous system

(sympathetic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Tumor necrosis factors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha., antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Adrenoceptor antagonists

(.alpha.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Adrenoceptor antagonists

(.beta.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 180384-56-9, Ro 61-1790

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Ro 61-1790; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 188307-16-6, T 0201

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(T 0201; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 52-39-1, Aldosterone

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(and aldosterone antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 9002-17-9, Xanthine oxidase 9004-08-4, Cathepsin 9015-82-1, Angiotensin-converting enzyme 9047-22-7, Cathepsin B 97501-92-3, Chymase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 9002-72-6, Growth hormone 67763-96-6, IGF-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 51-34-3, Scopolamine 52-01-7, Spironolactone 52-01-7D, Spironolactone, 15,16-methylene derivs. 57-27-2, Morphine, biological studies 60-26-4, Hexamethonium 60-30-0, Azamethonium 60-40-2, Mecamylamine 68-91-7 71-91-0, Tetraethylammonium bromide 100-33-4, Pentamidine 119-44-8, Xanthopterin 125-28-0, Dihydrocodeine 144-44-5, Pentolinium 315-30-0, Allopurinol 382-82-1 492-11-5, Leukopterin 497-23-4, 2(5H)-Furanone 525-66-6, Propranolol 546-48-5, Synapleg 555-30-6, .alpha.-Methyldopa 561-27-3, Diamorphine 968-93-4, Testolactone 971-60-8, Benzohexonium 1218-98-0, 7,8-Dihydroneopterin 2009-64-5, Neopterin 2365-25-5, Pentamethonium 2465-59-0, Oxypurinol 3613-69-2, Cypenam 3930-20-9, Sotalol 4138-96-9 4205-90-7, Clonidine 4844-10-4, Hexafluorenium 5472-41-3, 4-Amino-6-hydroxypyrazolo[3,4-d]pyrimidine 6452-71-7, Oxprenolol 7187-66-8, Trimetaphan 9087-70-1, Aprotinin 11096-26-7, Erythropoietin 13523-86-9, Pindolol 13655-52-2, Alprenolol 17528-72-2 19216-56-9, Prazosin 22150-76-1, Biopterin 22664-55-7, Metipranolol 26839-75-8, Timolol 29122-68-7, Atenolol 36894-69-6 37517-30-9, Acebutolol 38363-40-5, Penbutolol 42200-33-9, Nadolol 47141-42-4, Levobunolol **51384-51-1**, **Metoprolol** 51781-06-7, Carteolol 52485-79-7, Buprenorphine 54187-04-1, Rilmenidine 56980-93-9, Celiprolol 63590-64-7, Terazosin 63659-18-7, Betaxolol 66376-36-1, Alendronate 66722-44-9 67392-87-4, Dihydrospirorenone 71119-11-4, Bucindolol 72956-09-3, Carvedilol 74191-85-8, Doxazosin 74220-07-8, Spirorenone 75438-57-2, Moxonidine 76676-33-0, RU26752 76684-89-4, E 64c 81147-92-4, Esmolol 86102-31-0, Tissue inhibitor of matrix metalloproteinase 87952-98-5, Mespirenone 91448-99-6, Cystatin C 93519-21-2 95847-70-4, Ipsapirone 107544-29-6, Stefin A **107724-20-9**, **Eplerenone** 118457-14-0, Nebivolol 134448-10-5, CA-074 136553-74-7, WS 7338B 136553-81-6, BQ123 144602-02-8, IRL 1038 145380-08-1, RU40555 151039-33-7, PD 142893 156161-89-6, BQ-788 157659-79-5, SB 209670 162117-90-0, S 0139 162412-70-6, PD 156707 171714-84-4, LU135252 173189-01-0, IRL 3461 173937-91-2, ABT-627 204326-22-7, PD 164333 223756-43-2, A-216546 264276-89-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 75847-73-3, Enalapril 114798-26-4, Losartan

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 51-41-2, Noradrenaline 51-43-4, Epinephrine 11128-99-7, Angiotensin II 123626-67-5, Endothelin 1

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

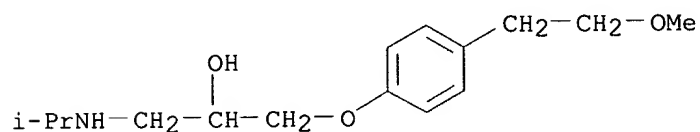
IT **51384-51-1, Metoprolol 107724-20-9, Eplerenone**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

RN 51384-51-1 HCAPLUS

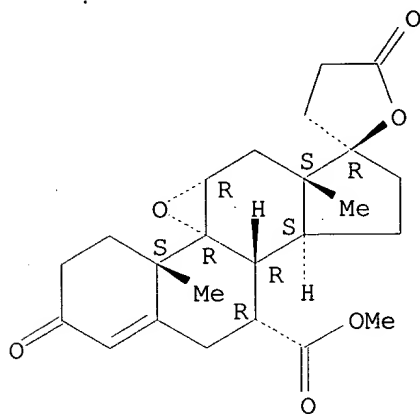
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)  
(CA INDEX NAME)



RN 107724-20-9 HCAPLUS

CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,  
.gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 15:17:42 ON 24 JUN 2003)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 15:17:54 ON 24 JUN 2003  
E METOPROLOL/CN

L1	1 S E3
	SEL RN
L2	29 S E1/CRN
L3	17 S L2 NOT MXS/CI
L4	229 S C15H25NO3/MF AND 46.150.18/RID AND 1/NR
L5	17 S L4 AND 2 PROPANOL AND 2 METHOXYETHYL PHENOXY
L6	13 S L5 NOT (D OR T)/ELS
L7	7 S L6 AND 4
	SEL RN
L8	14 S E2-E8/CRN NOT L2
L9	13 S L8 NOT MXS/CI
L10	7 S L9 NOT COMPD
L11	31 S L1,L3,L7,L10
L12	22 S L11 NOT (COMPD OR WITH)
L13	21 S L12 NOT 11C

L14 10 S L11 NOT L13

FILE 'HCAPLUS' ENTERED AT 15:23:45 ON 24 JUN 2003

L15 2799 S L13  
L16 3247 S METOPROLOL OR BEATROLOL OR SPESICOR OR CGP2175 OR CGP 2175  
L17 3560 S L15,L16  
E ALEXANDER J/AU  
L18 320 S E3,E8-E10  
E ALEXANDER JOHN/AU  
L19 29 S E3,E10-E12  
E SCHUH J/AU  
L20 53 S E3,E6,E14,E17,E18,E21,E22  
L21 1 S L17 AND L18-L20

FILE 'REGISTRY' ENTERED AT 15:25:56 ON 24 JUN 2003

L22 1 S EPLERENONE/CN  
L23 36 S 107724-20-9/CRN

FILE 'HCAPLUS' ENTERED AT 15:27:15 ON 24 JUN 2003

L24 67 S L22  
L25 8 S L23  
L26 81 S EPLERENONE OR SC66110 OR SC() (66110 OR 66 110) OR CGP30083 OR  
L27 92 S L24-L26  
L28 7 S L27 AND L18-L20  
L29 1 S L21 AND L28  
L30 1 S US20020123485/PN  
E WO2001-US23670/AP, PRN  
L31 1 S E3,E4  
E US2000-221365/AP, PRN  
L32 1 S E5  
L33 1 S L29-L32  
SEL RN

FILE 'REGISTRY' ENTERED AT 15:29:09 ON 24 JUN 2003

L34 80 S E1-E80  
L35 2 S L34 AND L22,L23  
L36 1 S L34 AND L13  
L37 16 S L34 AND NR>=5  
L38 12 S L34 AND NR>=6  
L39 16 S L37,L38  
L40 63 S L34 NOT L35-L39  
L41 3 S L39 AND K/ELS  
L42 11 S L38 NOT L41  
L43 10 S L42 AND 1/NC  
L44 STR  
L45 50 S L44  
L46 STR L44  
L47 18 S L46  
L48 STR L46  
L49 50 S L48  
L50 SCR 1851  
L51 50 S L48 AND L50  
L52 1341 S L48 AND L50 FUL  
SAV L52 QAZI917/A  
L53 STR  
L54 22 S L53 SAM SUB=L52  
L55 10 S L34 AND L52  
L56 6 S L39 NOT L55  
L57 554 S L53 FUL SUB=L52  
SAV L57 QAZI917A/A  
L58 552 S L57 NOT (CCS OR RIS OR PMS)/CI

FILE 'HCAPLUS' ENTERED AT 15:52:30 ON 24 JUN 2003

L59 67 S L55  
L60 4 S L59 AND L17

FILE 'REGISTRY' ENTERED AT 15:53:12 ON 24 JUN 2003  
L61 5 S L56 NOT C24H32O4S

FILE 'HCAPLUS' ENTERED AT 15:53:50 ON 24 JUN 2003  
L62 2 S L61  
L63 1 S L62 AND L17  
L64 4 S L27 AND L17  
L65 4 S L33,L60,L63,L64  
L66 360 S L58  
L67 4 S L66 AND L17  
L68 4 S L65,L67

FILE 'REGISTRY' ENTERED AT 15:56:48 ON 24 JUN 2003

FILE 'HCAPLUS' ENTERED AT 15:57:22 ON 24 JUN 2003

FILE 'MEDLINE' ENTERED AT 15:57:55 ON 24 JUN 2003  
L69 4457 S L17  
L70 75 S L27  
L71 1 S L69 AND L70  
L72 5 S EPOXYMEXRENONE  
L73 1 S L69 AND L72  
L74 1 S L71,L73

FILE 'EMBASE' ENTERED AT 15:59:01 ON 24 JUN 2003  
L75 13961 S L17  
L76 146 S L27 OR L72  
L77 8 S L75 AND L76  
L78 787 S L17(L)CB/CT  
L79 24 S L76(L)CB/CT  
L80 0 S L77 AND L78,L79

FILE 'WPIX' ENTERED AT 16:01:38 ON 24 JUN 2003  
L81 184 S L16/BIX  
E METOPROLOL/DCN  
E E3+ALL  
L82 134 S E2  
L83 63 S E4  
L84 11 S E6  
L85 12 S E8  
L86 24 S E10  
L87 1 S E12  
L88 3 S E14  
L89 242 S L81-L88  
L90 20 S L26/BIX  
L91 3 S L72/BIX  
E EPLERENONE/DCN  
E EPOXYMEXRENONE/DCN  
L92 3 S L89 AND L90,L91

=> fil medline

FILE 'MEDLINE' ENTERED AT 16:05:34 ON 24 JUN 2003

FILE LAST UPDATED: 21 JUN 2003 (20030621/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.



This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all 174

L74 ANSWER 1 OF 1 MEDLINE  
 AN 2000501947 MEDLINE  
 DN 20503076 PubMed ID: 11048403  
 TI [Cardiology at the end of the 20th century].  
 Kardiologie na konci 20. stoleti.  
 AU Jerie P  
 SO CASOPIS LEKARU CESKYCH, (2000 Jul 19) 139 (14) 422-5.  
 Journal code: 0004743. ISSN: 0008-7335.  
 CY Czech Republic  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA Czech  
 FS Priority Journals  
 EM 200011  
 ED Entered STN: 20010322  
 Last Updated on STN: 20010322  
 Entered Medline: 20001121  
 AB In autumn 1999 results of two well-controlled studies were published that are consistent with a frequent association between *Helicobacter pylori* seropositivity and coronary heart disease (CHD). Concerning the therapy of CHD, attention is mainly focused on new thrombolytic agents, bypass grafting (CABG) and balloon angioplasty (PTCA). In patients with intractable angina where aggressive medical therapy was exhausted and who were no longer candidates for CABG or PTCA, transmural laser revascularisation (TMLR), enhanced external counterpulsation (EECP) and spinal cord stimulation can be considered. TMLR was shown to improve symptoms but not myocardial perfusion; the preoperative mortality accounts for 10-20%. In hypertrophic obstructive cardiomyopathy, alcohol-induced transmural septal myocardial ablation (PTSMA) reduces both the symptoms and the left ventricular outflow tract gradient. Although the prevalence of hypertension emergencies has dramatically diminished, the number of hypertensive patients with heart failure and end-stage renal disease is increasing. It is important to detect and treat mild hypertensives in early stages, especially diabetics and younger women with additional risk factors and/or proteinuria. The choice and dosage of drugs is to be individualised. In chronic heart failure (CHF), the protective effect of ACE inhibitors, **metoprolol** and **carvedilol** has been repeatedly shown in CHF stage NYHA II and III. The merit of ACE inhibitor and beta-blockers in high doses remains questionable in old patients and those with severe CHF (NYHA IV). In the latter indication, spiro lactone was successfully reintroduced. **Eplerenone (epoxymexrenone)** is a new aldosterone antagonist with little affinity to other steroid receptors and has therefore less undesirable effects than spiro lactone. The body of knowledge in therapeutic and technical progress in medicine of the 20th century are summarised and their positive and negative consequences briefly discussed.  
 CT Check Tags: Human  
 \*Cardiology  
 English Abstract

=> fil embase

FILE 'EMBASE' ENTERED AT 16:05:50 ON 24 JUN 2003

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FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot 177

L77 ANSWER 1 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 AN 2003214503 EMBASE  
 TI New developments in the pharmacological treatment of chronic heart failure.  
 AU Krum H.; Liew D.  
 CS Dr. H. Krum, NH/MRC Ctr. Clin. Res. Excellence, Department of Medicine, Monash Univ. Ctrl./E. Clin. School, Melbourne, Vic. 3004, Australia. henry.krum@med.monash.edu.au  
 SO Expert Opinion on Investigational Drugs, (1 May 2003) 12/5 (751-757).  
 Refs: 57  
 ISSN: 1354-3784 CODEN: EOIDER  
 CY United Kingdom  
 DT Journal; General Review  
 FS 005 General Pathology and Pathological Anatomy  
 018 Cardiovascular Diseases and Cardiovascular Surgery  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LA English  
 SL English  
 AB In recent years, rapid growth in the understanding of the pathophysiology of chronic heart failure has allowed for insights into many potential new therapeutic strategies. Yet until now, despite sound biological basis for efficacy and success in early-Phase studies, novel agents have not stood up to the scrutiny of late-Phase clinical trials. Indeed, remarkably negative results have been observed for vasoactive peptide inhibitors, endothelin receptor antagonists and agents which block immune activation. However, efficacy data from other novel agents are still awaited, including the selective aldosterone receptor antagonist **eplerenone**, arginine vasopressin inhibitors, erythropoietin and hydroxy-methyl-glutaryl coenzyme A reductase inhibitors. Other classes of drugs which may enter clinical development include cardiac metabolic agents, matrix metalloproteinase inhibitors and advanced glycation end product antagonists. That the mortality and morbidity of patients with chronic heart failure remain unacceptably high makes the ongoing commitment to exploration of new drug therapies for the condition critical.  
 CT Medical Descriptors:  
 \*heart failure: DT, drug therapy  
 \*heart failure: ET, etiology  
 pathophysiology  
 drug efficacy  
 mortality  
 morbidity  
 heart muscle metabolism  
 enzyme inhibition  
 beta adrenergic receptor blocking  
 immunosuppressive treatment  
 drug synthesis  
 gynecomastia: SI, side effect  
 angioneurotic edema: SI, side effect  
 body weight disorder: SI, side effect  
 chronic disease  
 human  
 nonhuman  
 clinical trial  
 review  
 Drug Descriptors:

\*cardiovascular agent: CT, clinical trial  
\*cardiovascular agent: DV, drug development  
\*cardiovascular agent: PD, pharmacology  
vasopeptidase inhibitor: AE, adverse drug reaction  
vasopeptidase inhibitor: CT, clinical trial  
vasopeptidase inhibitor: CM, drug comparison  
vasopeptidase inhibitor: DT, drug therapy  
vasopeptidase inhibitor: PD, pharmacology  
endothelin receptor antagonist: AE, adverse drug reaction  
endothelin receptor antagonist: CT, clinical trial  
endothelin receptor antagonist: CM, drug comparison  
endothelin receptor antagonist: DO, drug dose  
endothelin receptor antagonist: DT, drug therapy  
endothelin receptor antagonist: PD, pharmacology  
aldosterone antagonist: AE, adverse drug reaction  
aldosterone antagonist: CT, clinical trial  
aldosterone antagonist: CB, drug combination  
aldosterone antagonist: CM, drug comparison  
aldosterone antagonist: DT, drug therapy  
aldosterone antagonist: PD, pharmacology  
  **eplerenone: AE, adverse drug reaction**  
  **eplerenone: CT, clinical trial**  
  **eplerenone: CM, drug comparison**  
  **eplerenone: DT, drug therapy**  
  **eplerenone: PD, pharmacology**  
argipressin: CT, clinical trial  
argipressin: DT, drug therapy  
argipressin: PD, pharmacology  
erythropoietin: CT, clinical trial  
erythropoietin: DT, drug therapy  
erythropoietin: PD, pharmacology  
hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial  
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy  
hydroxymethylglutaryl coenzyme A reductase inhibitor: PD, pharmacology  
matrix metalloproteinase inhibitor: DV, drug development  
matrix metalloproteinase inhibitor: PD, pharmacology  
advanced glycation end product: DV, drug development  
advanced glycation end product: PD, pharmacology  
dipeptidyl carboxypeptidase inhibitor: CT, clinical trial  
dipeptidyl carboxypeptidase inhibitor: CB, drug combination  
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison  
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology  
spironolactone: AE, adverse drug reaction  
spironolactone: CT, clinical trial  
spironolactone: CB, drug combination  
spironolactone: CM, drug comparison  
spironolactone: DT, drug therapy  
spironolactone: PD, pharmacology  
beta adrenergic receptor blocking agent: CM, drug comparison  
beta adrenergic receptor blocking agent: DT, drug therapy  
beta adrenergic receptor blocking agent: PD, pharmacology  
carvedilol: CT, clinical trial  
carvedilol: CB, drug combination  
carvedilol: CM, drug comparison  
carvedilol: DT, drug therapy  
carvedilol: PD, pharmacology  
  **metoprolol: CT, clinical trial**  
  **metoprolol: CM, drug comparison**  
  **metoprolol: DT, drug therapy**  
  **metoprolol: PD, pharmacology**  
enalapril: CT, clinical trial  
enalapril: CB, drug combination

enalapril: CM, drug comparison  
 enalapril: DT, drug therapy  
 enalapril: PD, pharmacology  
 nebivolol: CT, clinical trial  
 nebivolol: DT, drug therapy  
 nebivolol: PD, pharmacology  
 valsartan: CT, clinical trial  
 valsartan: DT, drug therapy  
 valsartan: PD, pharmacology  
 omapatrilat: AE, adverse drug reaction  
 omapatrilat: CM, drug comparison  
 omapatrilat: DT, drug therapy  
 omapatrilat: PD, pharmacology  
 bosentan: AE, adverse drug reaction  
 bosentan: CT, clinical trial  
 bosentan: DO, drug dose  
 bosentan: DT, drug therapy  
 bosentan: PD, pharmacology  
 enrasentan: AE, adverse drug reaction  
 enrasentan: CT, clinical trial  
 enrasentan: CM, drug comparison  
 enrasentan: DT, drug therapy  
 enrasentan: PD, pharmacology  
 darusentan: AE, adverse drug reaction  
 darusentan: CT, clinical trial  
 darusentan: CM, drug comparison  
 darusentan: DT, drug therapy  
 darusentan: PD, pharmacology  
 endothelin converting enzyme inhibitor: DV, drug development  
 recombinant tumor necrosis factor alpha: AE, adverse drug reaction  
 recombinant tumor necrosis factor alpha: CT, clinical trial  
 recombinant tumor necrosis factor alpha: CM, drug comparison  
 recombinant tumor necrosis factor alpha: DT, drug therapy  
 recombinant tumor necrosis factor alpha: PD, pharmacology  
 etanercept: AE, adverse drug reaction  
 etanercept: CT, clinical trial  
 etanercept: CM, drug comparison  
 etanercept: DT, drug therapy  
 etanercept: PD, pharmacology  
 infliximab: AE, adverse drug reaction  
 infliximab: CT, clinical trial  
 infliximab: CM, drug comparison  
 infliximab: DT, drug therapy  
 infliximab: PD, pharmacology  
 conivaptan: CT, clinical trial  
 conivaptan: DT, drug therapy  
 conivaptan: PD, pharmacology  
 rosuvastatin: CT, clinical trial  
 rosuvastatin: DT, drug therapy  
 rosuvastatin: PD, pharmacology  
 etomoxir: CT, clinical trial  
 etomoxir: DV, drug development  
 etomoxir: DT, drug therapy  
 etomoxir: PD, pharmacology  
 unindexed drug

RN (eplerenone) 107724-20-9; (argipressin) 113-79-1;  
 (erythropoietin) 11096-26-7; (spironolactone) 52-01-7; (carvedilol)  
 72956-09-3; (metoprolol) 37350-58-6; (enalapril)  
 75847-73-3; (nebivolol) 99200-09-6; (valsartan) 137862-53-4; (omapatrilat)  
 167305-00-2; (bosentan) 147536-97-8, 157212-55-0; (enrasentan)  
 167256-08-8, 183507-63-3; (darusentan) 171714-84-4; (etanercept)  
 185243-69-0, 200013-86-1; (infliximab) 170277-31-3; (conivaptan)  
 168626-94-6, 210101-16-9; (rosuvastatin) 147098-18-8, 147098-20-2;

(etomoxir) 82258-36-4

L77 ANSWER 2 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
AN 2003077160 EMBASE  
TI The pharmacological management of heart failure: Too many treatments?.  
AU Van Veldhuisen D.J.; Van Gilst W.H.  
CS D.J. Van Veldhuisen, Department of Cardiology, Thoraxcenter, University  
Hospital Groningen, P.O. Box 30.001, 9700 RB Groningen, Netherlands  
SO European Journal of Heart Failure, (2003) 5/1 (5-8).  
Refs: 36  
ISSN: 1388-9842 CODEN: EJHFFS  
PUI S 1388-9842(02)00159-9  
CY Netherlands.  
DT Journal; Editorial  
FS 018 Cardiovascular Diseases and Cardiovascular Surgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LA English  
CT Medical Descriptors:  
\*heart failure: DT, drug therapy  
heart hemodynamics  
mortality  
enzyme inhibition  
drug mechanism  
drug efficacy  
clinical research  
side effect: SI, side effect  
human  
clinical trial  
meta analysis  
editorial  
priority journal  
Drug Descriptors:  
\*digoxin: CT, clinical trial  
\*digoxin: DT, drug therapy  
\*diuretic agent: CT, clinical trial  
\*diuretic agent: DT, drug therapy  
\*dipeptidyl carboxypeptidase inhibitor: CT, clinical trial  
\*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
\*enalapril: CT, clinical trial  
\*enalapril: DT, drug therapy  
phosphodiesterase inhibitor: CT, clinical trial  
phosphodiesterase inhibitor: DT, drug therapy  
milrinone: CT, clinical trial  
milrinone: DT, drug therapy  
enoximone: CT, clinical trial  
enoximone: DT, drug therapy  
calcium sensitizer: CT, clinical trial  
calcium sensitizer: DT, drug therapy  
pimobendan: CT, clinical trial  
pimobendan: DT, drug therapy  
calcium antagonist: CT, clinical trial  
calcium antagonist: DT, drug therapy  
felodipine: CT, clinical trial  
felodipine: DT, drug therapy  
amlodipine: CT, clinical trial  
amlodipine: DT, drug therapy  
dopamine receptor stimulating agent: CT, clinical trial  
dopamine receptor stimulating agent: DT, drug therapy  
ibopamine: CT, clinical trial  
ibopamine: DT, drug therapy  
vasodilator agent: CT, clinical trial  
vasodilator agent: DT, drug therapy

flosequinan: CT, clinical trial  
 flosequinan: DT, drug therapy  
 prostacyclin: CT, clinical trial  
 prostacyclin: DT, drug therapy  
 beta adrenergic receptor blocking agent: CT, clinical trial  
 beta adrenergic receptor blocking agent: DT, drug therapy  
 bisoprolol: CT, clinical trial  
 bisoprolol: DT, drug therapy  
     **metoprolol: CT, clinical trial**  
     **metoprolol: DT, drug therapy**  
 angiotensin receptor antagonist: CT, clinical trial  
 angiotensin receptor antagonist: DT, drug therapy  
 losartan: CT, clinical trial  
 losartan: DT, drug therapy  
 captopril: CT, clinical trial  
 captopril: DT, drug therapy  
 valsartan: CT, clinical trial  
 valsartan: DT, drug therapy  
 aldosterone antagonist: CT, clinical trial  
 aldosterone antagonist: DT, drug therapy  
 spironolactone: AE, adverse drug reaction  
 spironolactone: CT, clinical trial  
 spironolactone: DT, drug therapy  
     **eplerenone: CT, clinical trial**  
     **eplerenone: DT, drug therapy**  
 endothelin receptor antagonist: CT, clinical trial  
 endothelin receptor antagonist: DT, drug therapy  
 vasopectidase inhibitor: CT, clinical trial  
 vasopectidase inhibitor: DT, drug therapy  
 unindexed drug

RN (digoxin) 20830-75-5, 57285-89-9; (enalapril) 75847-73-3; (milrinone)  
 78415-72-2; (enoximone) 77671-31-9; (pimobendan) 74150-27-9; (felodipine)  
 72509-76-3; (amlodipine) 88150-42-9; (ibopamine) 66195-31-1, 75011-65-3;  
 (flosequinan) 76568-02-0; (prostacyclin) 35121-78-9, 61849-14-7;  
 (bisoprolol) 66722-44-9; (**metoprolol**) **37350-58-6**;  
 (losartan) 114798-26-4; (captopril) 62571-86-2; (valsartan) 137862-53-4;  
 (spironolactone) 52-01-7; (**eplerenone**) **107724-20-9**

L77 ANSWER 3 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2003004084 EMBASE

TI Update from the International Society on Hypertension in Blacks.

AU McCullough P.A.

CS Dr. P.A. McCullough, Div. Nutrition/Preventive Medicine, William Beaumont  
Hospital, Royal Oak, MI, United States

SO Reviews in Cardiovascular Medicine, (2002) 3/4 (192-195).

Refs: 7

ISSN: 1530-6550 CODEN: RCMEC5

CY United States

DT Journal; Conference Article

FS 006 Internal Medicine

017 Public Health, Social Medicine and Epidemiology

018 Cardiovascular Diseases and Cardiovascular Surgery

028 Urology and Nephrology

037 Drug Literature Index

LA English

CT Medical Descriptors:

\*hypertension: DT, drug therapy

\*hypertension: EP, epidemiology

\*hypertension: PC, prevention

medical society

ethnic group

risk factor

cardiovascular risk

chronic kidney disease  
 cardiovascular disease: CO, complication  
 kidney failure  
 heart infarction  
 heart failure  
 heart arrest  
 patient care  
 diabetic nephropathy  
 renin angiotensin aldosterone system  
 blood pressure regulation  
 patient compliance  
 blood pressure monitoring  
 comorbidity  
 human  
 conference paper  
 Drug Descriptors:  
 low density lipoprotein: EC, endogenous compound  
 cholesterol: EC, endogenous compound  
 ramipril: CM, drug comparison  
 ramipril: DT, drug therapy  
     **metoprolol: CM, drug comparison**  
     **metoprolol: DT, drug therapy**  
 amlodipine: CM, drug comparison  
 amlodipine: DT, drug therapy  
 dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
 hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy  
 aldosterone receptor: EC, endogenous compound  
 aldosterone antagonist: DT, drug therapy  
     **eplerenone: DT, drug therapy**  
 placebo  
 aldosterone: EC, endogenous compound  
 renin: EC, endogenous compound  
 RN (cholesterol) 57-88-5; (ramipril) 87333-19-5; (**metoprolol**)  
 37350-58-6; (amlodipine) 88150-42-9; (**eplerenone**)  
 107724-20-9; (aldosterone) 52-39-1, 6251-69-0; (renin) 61506-93-2,  
 9015-94-5

L77 ANSWER 4 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 AN 2002422728 EMBASE  
 TI Clinical treatment regimens for chronic heart failure: A review.  
 AU Gould P.A.; Kaye D.M.  
 CS P.A. Gould, Alfred Heart Centre, Commercial Rd., Prahran, Vic. 3181,  
 Australia. d.kaye@alfred.org.au  
 SO Expert Opinion on Pharmacotherapy, (1 Nov 2002) 3/11 (1569-1576).  
 Refs: 56  
 ISSN: 1465-6566 CODEN: EOPHF7  
 CY United Kingdom  
 DT Journal; General Review  
 FS 017 Public Health, Social Medicine and Epidemiology  
 018 Cardiovascular Diseases and Cardiovascular Surgery  
 027 Biophysics, Bioengineering and Medical Instrumentation  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LA English  
 SL English  
 AB Chronic heart failure (CHF) is increasing in prevalence worldwide,  
 particularly in the elderly. Accordingly, this epidemic is likely to  
 translate into a major increase in healthcare costs. Systolic heart  
 failure is the most common cause of CHF presentations. Although the causes  
 vary, the most common single aetiological factor is ischaemic heart  
 disease, which accounts for .apprx. 50% of heart failure presentations.  
 Research into CHF pharmacotherapy has been copious, with the focus

principally centred on systolic heart failure. The evidence base for pharmacotherapy in CHF is amongst the largest currently in clinical medicine. There have been multiple trials establishing the mortality and morbidity benefits of pharmacotherapy. Amongst these, large scale trials of angiotensin-converting enzyme inhibitors, .beta.-blockers and spironolactone have provided a sound basis for evidence-based treatment approaches to the CHF patient. Recently research interest has increased in biomedical engineering with studies being performed in biventricular pacing and mechanical hearts. Early data with biventricular pacing or cardiac resynchronisation therapy is encouraging. Diastolic heart failure alone accounts for at least 20 - 40% of CHF presentations and whilst it may occur in isolation, is most commonly seen in association with systolic heart failure. In this study, we present a broad overview of the current therapeutic modalities for the management of CHF, with particular emphasis on pharmacotherapy.

#### CT Medical Descriptors:

\*heart failure: CO, complication  
 \*heart failure: DI, diagnosis  
 \*heart failure: DT, drug therapy  
 \*heart failure: EP, epidemiology  
 \*heart failure: ET, etiology  
 \*heart failure: SU, surgery  
 treatment planning  
 chronic disease  
 prevalence  
 epidemic  
 health care cost  
 systole  
 ischemic heart disease  
 clinical medicine  
 mortality  
 morbidity  
 clinical research  
 biomedical engineering  
 heart pacing  
 artificial heart  
 diastole  
 patient care  
 optimal drug dose  
 coughing: SI, side effect  
 angioneurotic edema: SI, side effect  
 slow release formulation  
 hypotension: SI, side effect  
 bradycardia: SI, side effect  
 drug bioavailability  
 hyperkalemia: SI, side effect  
 human  
 controlled study  
 aged  
 review

#### Drug Descriptors:

dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction  
 dipeptidyl carboxypeptidase inhibitor: CB, drug combination  
 dipeptidyl carboxypeptidase inhibitor: CM, drug comparison  
 dipeptidyl carboxypeptidase inhibitor: DO, drug dose  
 dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
 dipeptidyl carboxypeptidase inhibitor: PD, pharmacology  
 beta adrenergic receptor blocking agent: AE, adverse drug reaction  
 beta adrenergic receptor blocking agent: CB, drug combination  
 beta adrenergic receptor blocking agent: DO, drug dose  
 beta adrenergic receptor blocking agent: DT, drug therapy  
 beta adrenergic receptor blocking agent: PD, pharmacology  
 spironolactone: AE, adverse drug reaction



spironolactone: CB, drug combination  
spironolactone: CM, drug comparison  
spironolactone: DO, drug dose  
spironolactone: DT, drug therapy  
spironolactone: PD, pharmacology  
angiotensin receptor antagonist: AE, adverse drug reaction  
angiotensin receptor antagonist: CB, drug combination  
angiotensin receptor antagonist: CM, drug comparison  
angiotensin receptor antagonist: DT, drug therapy  
angiotensin receptor antagonist: PD, pharmacology  
losartan potassium: CB, drug combination  
losartan potassium: CM, drug comparison  
losartan potassium: DT, drug therapy  
losartan potassium: PD, pharmacology  
captopril: CB, drug combination  
captopril: CM, drug comparison  
captopril: DO, drug dose  
captopril: DT, drug therapy  
captopril: PD, pharmacology  
enalapril: CM, drug comparison  
enalapril: DO, drug dose  
enalapril: DT, drug therapy  
lisinopril: CM, drug comparison  
lisinopril: DO, drug dose  
lisinopril: DT, drug therapy  
ramipril: CM, drug comparison  
ramipril: DO, drug dose  
ramipril: DT, drug therapy  
quinapril: CM, drug comparison  
quinapril: DO, drug dose  
quinapril: DT, drug therapy  
trandolapril: CM, drug comparison  
trandolapril: DO, drug dose  
trandolapril: DT, drug therapy  
perindopril: CM, drug comparison  
perindopril: DO, drug dose  
perindopril: DT, drug therapy  
carvedilol: AE, adverse drug reaction  
carvedilol: DO, drug dose  
carvedilol: DT, drug therapy  
carvedilol: PD, pharmacology  
bisoprolol: DT, drug therapy  
bisoprolol: PD, pharmacology  
    **metoprolol: DO, drug dose**  
    **metoprolol: DT, drug therapy**  
    **metoprolol: PR, pharmaceuticals**  
    **metoprolol: PD, pharmacology**  
bisoprolol fumarate: DO, drug dose  
bisoprolol fumarate: DT, drug therapy  
diuretic agent: AE, adverse drug reaction  
diuretic agent: CB, drug combination  
diuretic agent: CM, drug comparison  
diuretic agent: DO, drug dose  
diuretic agent: DT, drug therapy  
diuretic agent: PK, pharmacokinetics  
diuretic agent: PD, pharmacology  
diuretic agent: IV, intravenous drug administration  
loop diuretic agent: CB, drug combination  
loop diuretic agent: CM, drug comparison  
loop diuretic agent: DT, drug therapy  
loop diuretic agent: PK, pharmacokinetics  
loop diuretic agent: PD, pharmacology  
thiazide diuretic agent: CB, drug combination

thiazide diuretic agent: CM, drug comparison  
 thiazide diuretic agent: DT, drug therapy  
 thiazide diuretic agent: PD, pharmacology  
 furosemide: CM, drug comparison  
 furosemide: DT, drug therapy  
 furosemide: PK, pharmacokinetics  
 furosemide: PD, pharmacology  
 torasemide: CM, drug comparison  
 torasemide: DT, drug therapy  
 torasemide: PK, pharmacokinetics  
 torasemide: PD, pharmacology  
 potassium sparing diuretic agent: AE, adverse drug reaction  
 potassium sparing diuretic agent: CB, drug combination  
 potassium sparing diuretic agent: CM, drug comparison  
 potassium sparing diuretic agent: DO, drug dose  
 potassium sparing diuretic agent: DT, drug therapy  
 potassium sparing diuretic agent: PD, pharmacology

**eplerenone: AE, adverse drug reaction**

**eplerenone: CM, drug comparison**

**eplerenone: DT, drug therapy**

**eplerenone: PD, pharmacology**

aldosterone antagonist: AE, adverse drug reaction

aldosterone antagonist: CM, drug comparison

aldosterone antagonist: DT, drug therapy

aldosterone antagonist: PD, pharmacology

digoxin: DT, drug therapy

digoxin: PD, pharmacology

cardiac glycoside: DT, drug therapy

cardiac glycoside: PD, pharmacology

hydralazine: CB, drug combination

hydralazine: CM, drug comparison

hydralazine: DT, drug therapy

hydralazine: PD, pharmacology

isosorbide dinitrate: CB, drug combination

isosorbide dinitrate: CM, drug comparison

isosorbide dinitrate: DT, drug therapy

isosorbide dinitrate: PD, pharmacology

verapamil: AE, adverse drug reaction

verapamil: DT, drug therapy

verapamil: PD, pharmacology

unindexed drug

- RN (spironolactone) 52-01-7; (losartan potassium) 124750-99-8; (captopril) 62571-86-2; (enalapril) 75847-73-3; (lisinopril) 76547-98-3, 83915-83-7; (ramipril) 87333-19-5; (quinapril) 82586-55-8, 85441-61-8; (trandolapril) 87679-37-6; (perindopril) 82834-16-0; (carvedilol) 72956-09-3; (bisoprolol) 66722-44-9; (**metoprolol**) **37350-58-6**; (bisoprolol fumarate) 104344-23-2; (furosemide) 54-31-9; (torasemide) 56211-40-6; (**eplerenone**) **107724-20-9**; (digoxin) 20830-75-5, 57285-89-9; (hydralazine) 304-20-1, 86-54-4; (isosorbide dinitrate) 87-33-2; (verapamil) 152-11-4, 52-53-9
- CN (1) Cozaar; (2) Captopril; (3) Toprol; (4) Zebeta; (5) Aldactone; (6) Lanoxin; (7) Calan
- CO (1) Merck; (2) Bristol Myers Squibb; (3) Astra Zeneca; (4) Lederle; (6) Glaxo SmithKline; (7) Searle

L77 ANSWER 5 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2002386267 EMBASE

TI Heart failure: New data and guidelines.

AU Keown M.L.; Rahko P.S.

CS Dr. P.S. Rahko, G7/343 CSC, Cardiovascular Medicine Section, University of Wisconsin Hospital, 600 Highland Ave, Madison, WI 53792-3248, United States. psr@medicine.wisc.edu

SO Wisconsin Medical Journal, (2002) 101/7 (16-23).

Refs: 48

ISSN: 1098-1861 CODEN: WMJOA7

CY United States

DT Journal; General Review

FS 006 Internal Medicine

018 Cardiovascular Diseases and Cardiovascular Surgery

027 Biophysics, Bioengineering and Medical Instrumentation

037 Drug Literature Index

LA English

SL English

AB Heart failure is a common clinical problem, affecting at least 5 million Americans. There have been substantial advances in the understanding and treatment of heart failure in the last several years. We review current concepts for the evaluation and treatment of the various manifestations of patients with heart failure.

CT Medical Descriptors:

\*heart failure: DI, diagnosis

\*heart failure: DT, drug therapy

\*heart failure: EP, epidemiology

\*heart failure: ET, etiology

\*heart failure: SU, surgery

\*heart failure: TH, therapy

United States

clinical feature

disease course

diastolic blood pressure

systolic blood pressure

algorithm

electrocardiogram

hypertension: DT, drug therapy

heart left ventricle filling pressure

patient education

drug indication

drug contraindication

positive end expiratory pressure

intubation

defibrillator

heart transplantation

human

clinical trial

review

Drug Descriptors:

\*diuretic agent: CT, clinical trial

\*diuretic agent: DO, drug dose

\*diuretic agent: DT, drug therapy

\*diuretic agent: IV, intravenous drug administration

\*vasodilator agent: DT, drug therapy

\*vasodilator agent: PD, pharmacology

\*hypertensive agent: DT, drug therapy

\*hypertensive agent: PD, pharmacology

\*aldosterone antagonist: DO, drug dose

\*aldosterone antagonist: DT, drug therapy

dipeptidyl carboxypeptidase inhibitor: DO, drug dose

dipeptidyl carboxypeptidase inhibitor: DT, drug therapy

angiotensin receptor antagonist: DT, drug therapy

beta adrenergic receptor blocking agent: CB, drug combination

beta adrenergic receptor blocking agent: DO, drug dose

beta adrenergic receptor blocking agent: DT, drug therapy

calcium channel blocking agent: CB, drug combination

calcium channel blocking agent: DT, drug therapy

verapamil: DT, drug therapy

diltiazem: DT, drug therapy

digoxin: CB, drug combination

digoxin: DO, drug dose  
 digoxin: DT, drug therapy  
 digoxin: PD, pharmacology  
 furosemide: DT, drug therapy  
 furosemide: IV, intravenous drug administration  
 metolazone: AD, drug administration  
 metolazone: DT, drug therapy  
 torasemide: CT, clinical trial  
 torasemide: DT, drug therapy  
 glyceryl trinitrate: DT, drug therapy  
 nitroprusside sodium: DT, drug therapy  
 nesiritide: DT, drug therapy  
 brain natriuretic peptide: DT, drug therapy  
 dobutamine: DT, drug therapy  
 dopamine: DT, drug therapy  
 carvedilol: DT, drug therapy  
**metoprolol: DT, drug therapy**  
 bisoprolol: DT, drug therapy  
 atenolol: DT, drug therapy  
 bucindolol: CT, clinical trial  
 bucindolol: DT, drug therapy  
 spironolactone: DO, drug dose  
 spironolactone: DT, drug therapy  
**epplerenone: DT, drug therapy**

RN (verapamil) 152-11-4, 52-53-9; (diltiazem) 33286-22-5, 42399-41-7;  
 (digoxin) 20830-75-5, 57285-89-9; (furosemide) 54-31-9; (metolazone)  
 17560-51-9; (torasemide) 56211-40-6; (glyceryl trinitrate) 55-63-0;  
 (nitroprusside sodium) 14402-89-2, 15078-28-1; (nesiritide) 124584-08-3,  
 189032-40-4; (brain natriuretic peptide) 114471-18-0; (dobutamine)  
 34368-04-2, 52663-81-7; (dopamine) 51-61-6, 62-31-7; (carvedilol)  
 72956-09-3; **(metoprolol) 37350-58-6**; (bisoprolol)  
 66722-44-9; (atenolol) 29122-68-7; (bucindolol) 71119-11-4;  
 (spironolactone) 52-01-7; **(epplerenone) 107724-20-9**

L77. ANSWER 6 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2002135044 EMBASE

TI Current treatment and future directions in heart failure.

AU Wells G.; Little W.C.

CS G. Wells, Cardiology Section, Wake Forest Univ. School of Medicine,  
 Medical Center Boulevard, Winston-Salem, NC 27157-1045, United States.  
 wlittle@wfubmc.edu

SO Current Opinion in Pharmacology, (1 Apr 2002) 2/2 (148-153).

Refs: 43

ISSN: 1471-4892 CODEN: COPUBK

CY United Kingdom

DT Journal; Article

FS 006 Internal Medicine

018 Cardiovascular Diseases and Cardiovascular Surgery

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

AB Recent research in the pathophysiology of congestive heart failure has  
 focused on the blockade of neurohormonal systems. Large clinical trials  
 have clearly demonstrated morbidity and mortality benefits of  
 angiotensin-converting-enzyme inhibitors and beta blockers. Indeed, all  
 patients with heart failure should be treated with these agents unless  
 there is a specific contraindication otherwise. Despite this treatment,  
 however, mortality from heart failure remains high. Current investigation  
 is now focused on other pathophysiological mechanisms and the interruption  
 of these pathways.

CT Medical Descriptors:

\*congestive heart failure: DT, drug therapy  
\*congestive heart failure: ET, etiology  
medical research  
pathophysiology  
morbidity  
mortality  
drug contraindication  
renin angiotensin aldosterone system  
drug tolerability  
side effect: SI, side effect  
gynecomastia: SI, side effect  
nephrotoxicity: SI, side effect  
angioneurotic edema: SI, side effect  
human  
controlled study  
article  
priority journal  
Drug Descriptors:  
\*dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction  
\*dipeptidyl carboxypeptidase inhibitor: CB, drug combination  
\*dipeptidyl carboxypeptidase inhibitor: CM, drug comparison  
\*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
\*dipeptidyl carboxypeptidase inhibitor: PD, pharmacology  
\*beta adrenergic receptor blocking agent: AE, adverse drug reaction  
\*beta adrenergic receptor blocking agent: CB, drug combination  
\*beta adrenergic receptor blocking agent: DT, drug therapy  
neurohormone: EC, endogenous compound  
dipeptidyl carboxypeptidase: EC, endogenous compound  
angiotensin receptor antagonist: AE, adverse drug reaction  
angiotensin receptor antagonist: CM, drug comparison  
angiotensin receptor antagonist: DT, drug therapy  
angiotensin receptor antagonist: PD, pharmacology  
losartan: AE, adverse drug reaction  
losartan: CM, drug comparison  
losartan: DT, drug therapy  
losartan: PD, pharmacology  
enalapril: AE, adverse drug reaction  
enalapril: CB, drug combination  
enalapril: CM, drug comparison  
enalapril: DT, drug therapy  
enalapril: PD, pharmacology  
valsartan: CB, drug combination  
valsartan: DT, drug therapy  
valsartan: PD, pharmacology  
candesartan: CB, drug combination  
candesartan: CM, drug comparison  
candesartan: PD, pharmacology  
aldosterone antagonist: AE, adverse drug reaction  
aldosterone antagonist: DT, drug therapy  
aldosterone antagonist: PD, pharmacology  
spironolactone: AE, adverse drug reaction  
spironolactone: DT, drug therapy  
spironolactone: PD, pharmacology  
loop diuretic agent: DT, drug therapy  
  eplerenone: AE, adverse drug reaction  
  eplerenone: DT, drug therapy  
  metoprolol: CM, drug comparison  
  metoprolol: DT, drug therapy  
  metoprolol: PD, pharmacology  
carvedilol: CM, drug comparison  
carvedilol: DT, drug therapy  
carvedilol: PD, pharmacology  
bisoprolol: DT, drug therapy

bisoprolol: PD, pharmacology  
 beta 2 adrenergic receptor blocking agent: CM, drug comparison  
 beta 2 adrenergic receptor blocking agent: DT, drug therapy  
 beta 2 adrenergic receptor blocking agent: PD, pharmacology  
 bucindolol: DT, drug therapy  
 bucindolol: PD, pharmacology  
 moxonidine: PD, pharmacology  
 endothelin: EC, endogenous compound  
 endothelin receptor antagonist: AE, adverse drug reaction  
 endothelin receptor antagonist: DO, drug dose  
 endothelin receptor antagonist: DT, drug therapy  
 endothelin receptor antagonist: PD, pharmacology  
 bosentan: AE, adverse drug reaction  
 bosentan: DO, drug dose  
 bosentan: DT, drug therapy  
 bosentan: PD, pharmacology  
 endothelin converting enzyme inhibitor: CB, drug combination  
 endothelin converting enzyme inhibitor: DT, drug therapy  
 endothelin converting enzyme inhibitor: PD, pharmacology  
 phosphoramidon: CB, drug combination  
 phosphoramidon: DT, drug therapy  
 phosphoramidon: PD, pharmacology  
 pentoxifylline: DT, drug therapy  
 pentoxifylline: PD, pharmacology  
 etanercept: DT, drug therapy  
 etanercept: PD, pharmacology  
 vasopeptidase inhibitor: DT, drug therapy  
 vasopeptidase inhibitor: PD, pharmacology  
 omapatrilat: AE, adverse drug reaction  
 omapatrilat: CM, drug comparison  
 omapatrilat: DT, drug therapy  
 omapatrilat: PD, pharmacology  
 lisinopril: AE, adverse drug reaction  
 lisinopril: CM, drug comparison  
 lisinopril: DT, drug therapy  
 lisinopril: PD, pharmacology  
 unindexed drug

RN (dipeptidyl carboxypeptidase) 9015-82-1; (losartan) 114798-26-4;  
 (enalapril) 75847-73-3; (valsartan) 137862-53-4; (candesartan)  
 139481-59-7; (spironolactone) 52-01-7; (**eplerenone**)  
**107724-20-9**; (**metoprolol**) **37350-58-6**;  
 (carvedilol) 72956-09-3; (bisoprolol) 66722-44-9; (bucindolol) 71119-11-4;  
 (moxonidine) 75438-57-2; (phosphoramidon) 36357-77-4; (pentoxifylline)  
 6493-05-6; (etanercept) 185243-69-0, 200013-86-1; (omapatrilat)  
 167305-00-2; (lisinopril) 76547-98-3, 83915-83-7

L77 ANSWER 7 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 AN 2000292848 EMBASE  
 TI [Cardiology update 1999].  
 KARDIOLOGIE NA KONCI 20. STOLETI.  
 AU Jerie P.  
 CS Dr. P. Jerie, Leymenstrasse 49, CH-4153 Reinach, BL, Switzerland  
 SO Casopis Lekarů Cesky, (2000) 139/14 (422-425).  
 Refs: 38  
 ISSN: 0008-7335 CODEN: CLCEAL  
 CY Czech Republic  
 DT Journal; General Review  
 FS 004 Microbiology  
 018 Cardiovascular Diseases and Cardiovascular Surgery  
 037 Drug Literature Index

LA Czech

SL English; Czech

AB In autumn 1999 results of two well-controlled studies were published that

are consistent with a frequent association between *Helicobacter pylori* seropositivity and coronary heart disease (CHD). Concerning the therapy of CHD, attention is mainly focused on new thrombolytic agents, bypass grafting (CABG) and balloon angioplasty (PTCA). In patients with intractable angina where aggressive medical therapy was exhausted and who were no longer candidates for CABG or PTCA, transmural laser revascularisation (TMLR), enhanced external counterpulsation (EECP) and spinal cord stimulation can be considered. TMLR was shown to improve symptoms but not myocardial perfusion; the preoperative mortality accounts for 10-20 %. In hypertrophic obstructive cardiomyopathy, alcohol-induced transmural septal myocardial ablation (PTSMA) reduces both the symptoms and the left ventricular outflow tract gradient. Although the prevalence of hypertension emergencies has dramatically diminished, the number of hypertensive patients with heart failure and end-stage renal disease is increasing. It is important to detect and treat mild hypertensives in early stages, especially diabetics and younger women with additional risk factors and/or proteinuria. The choice and dosage of drugs is to be individualised. In chronic heart failure (CHF), the protective effect of ACE inhibitors, **metoprolol** and carvedilol has been repeatedly shown in CHF stage NYHA II and III. The merit of ACE inhibitor and  $\beta$ -blockers in high doses remains questionable in old patients and those with severe CHF (NYHA IV). In the latter indication, spironolactone was successfully reintroduced. **Eplerenone** (**epoxymexrenone**) is a new aldosterone antagonist with little affinity to other steroid receptors and has therefore less undesirable effects than spironolactone. The body of knowledge in therapeutic and technical progress in medicine of the 20th century are summarised and their positive and negative consequences briefly discussed.

CT Medical Descriptors:

\**Helicobacter pylori*  
 \*ischemic heart disease: DT, drug therapy  
 \*heart failure: DT, drug therapy  
 serodiagnosis  
 coronary artery bypass graft  
 transluminal coronary angioplasty  
 revascularization  
 spinal cord stimulation  
 heart muscle perfusion  
 disease association  
 hypertension  
 risk factor  
 treatment indication  
 human  
 review

Drug Descriptors:

\*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
 \*dipeptidyl carboxypeptidase inhibitor: PD, pharmacology  
 \*beta adrenergic receptor blocking agent: DT, drug therapy  
 \*beta adrenergic receptor blocking agent: PD, pharmacology  
 spironolactone: DT, drug therapy  
 spironolactone: PD, pharmacology  
     **eplerenone: DT, drug therapy**  
     **metoprolol: DT, drug therapy**  
     **metoprolol: PD, pharmacology**  
 carvedilol: DT, drug therapy  
 carvedilol: PD, pharmacology

RN (spironolactone) 52-01-7; (**eplerenone**) 107724-20-9; (**metoprolol**) 37350-58-6; (carvedilol) 72956-09-3

L77 ANSWER 8 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 1999281540 EMBASE

TI Recent progress in the treatment of hypertension and related disorders.

AU Cases A.

CS Dr. A. Cases, Dept. of Nephrology, Hospital Clinic, Villarroel 170, 08036  
Barcelona, Spain

SO Drug News and Perspectives, (1999) 12/6 (372-377).  
ISSN: 0214-0934 CODEN: DNPEED

CY Spain

DT Journal; Conference Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index

LA English

SL English

AB The 14th Annual Scientific Meeting of the American Society of  
Hypertension, held in New York, May 19-22, 1999, presented recent advances  
in the field of hypertension and related cardiovascular disorders.  
Presenters discussed the evidence for the beneficial effects of the use of  
.beta.-blockers in terms of mortality in patients with heart failure. The  
possible usefulness of endothelin antagonists in hypertension and heart  
failure was also discussed. The overall results of three phase II trials  
on the antihypertensive efficacy and tolerability of the dual  
vasopeptidase inhibitor omapatrilat were presented during the meeting. The  
antihypertensive effects and tolerability of members of the new class of  
11 imidazoline receptor agonists (rilmenidine and moxonidine) were  
reviewed in a satellite symposium and an invited lecture. The beneficial  
use of antialdosterone agents, such as spironolactone, in patients with  
severe heart failure and the recent development of more selective  
aldosterone receptor antagonists (SARAs), such as **eplerenone** -  
currently under investigation in hypertension and heart failure - were  
also presented during the meeting.

CT Medical Descriptors:  
\*hypertension: DT, drug therapy  
\*cardiovascular disease: DT, drug therapy  
heart failure  
drug efficacy  
drug tolerability  
drug structure  
human  
clinical trial  
phase 2 clinical trial  
meta analysis  
conference paper  
Drug Descriptors:  
\*beta adrenergic receptor blocking agent: CT, clinical trial  
\*beta adrenergic receptor blocking agent: AN, drug analysis  
\*beta adrenergic receptor blocking agent: DT, drug therapy  
\*endothelin receptor antagonist: AN, drug analysis  
\*endothelin receptor antagonist: DT, drug therapy  
\*endothelin receptor antagonist: PD, pharmacology  
\*membrane metalloendopeptidase: CT, clinical trial  
\*membrane metalloendopeptidase: DT, drug therapy  
\*membrane metalloendopeptidase: PD, pharmacology  
\*omapatrilat: CT, clinical trial  
\*omapatrilat: AN, drug analysis  
\*omapatrilat: DT, drug therapy  
\*omapatrilat: PD, pharmacology  
endothelin 1: EC, endogenous compound  
bosentan: AN, drug analysis  
bosentan: DT, drug therapy  
bosentan: PD, pharmacology  
rilmenidine: AN, drug analysis  
rilmenidine: DT, drug therapy  
moxonidine: AN, drug analysis  
moxonidine: DT, drug therapy  
moxonidine: PD, pharmacology



spironolactone: CT, clinical trial  
 spironolactone: AN, drug analysis  
 spironolactone: DT, drug therapy  
 aldosterone antagonist: AN, drug analysis  
 aldosterone antagonist: DT, drug therapy

**eplerenone: AN, drug analysis**

**eplerenone: DT, drug therapy**

bucindolol: CT, clinical trial

bucindolol: DT, drug therapy

carvedilol: AN, drug analysis

carvedilol: DT, drug therapy

**metoprolol: CT, clinical trial**

**metoprolol: AN, drug analysis**

**metoprolol: DT, drug therapy**

bisoprolol: CT, clinical trial

bisoprolol: AN, drug analysis

bisoprolol: DT, drug therapy

RN (membrane metalloendopeptidase) 82707-54-8, 88201-55-2; (rilmenidine)  
 54187-04-1; (moxonidine) 75438-57-2; (spironolactone) 52-01-7;  
 (bucindolol) 71119-11-4; (carvedilol) 72956-09-3; (**metoprolol**)  
**37350-58-6**; (bisoprolol) 66722-44-9

=> fil wpix

FILE 'WPIX' ENTERED AT 16:06:03 ON 24 JUN 2003

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 MOST RECENT DERWENT UPDATE: 200340 <200340/DW>  
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 /BIX is also provided which comprises both /BI and /ABEX <<<

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L92 ANSWER 1 OF 3 WPIX (C) 2003 THOMSON DERWENT

AN 2003-075655 [07] WPIX

DNC C2003-019682

TI Use of new and known probucol monoester compounds for increasing high  
 density lipoprotein cholesterol level used for treating cardiovascular  
 diseases.

DC B05

IN LUCHOONUN, J; SAXENA, U; SIKORSKI, J A; SUNDELL, C L

PA (LUCH-I) LUCHOONUN J; (SAXE-I) SAXENA U; (SIKO-I) SIKORSKI J A; (SUND-I)  
 SUNDELL C L; (ATHE-N) ATHEROGENICS INC

CYC 100

PI WO 2002087556 A2 20021107 (200307)\* EN 161p A61K031-00  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
 ZW

US 2003064967 A1 20030403 (200325) A61K031-66

ADT WO 2002087556 A2 WO 2002-US12678 20020411; US 2003064967 A1 Provisional US  
 2001-283376P 20010411, Provisional US 2001-345025P 20011109, US  
 2002-122516 20020411

PRAI US 2001-345025P 20011109; US 2001-283376P 20010411; US 2002-122516  
 20020411

IC ICM A61K031-00; A61K031-66  
 ICS A61K031-255; A61K031-397; A61K031-40; A61K031-445

AB WO 200287556 A UPAB: 20030129  
 NOVELTY - Use of probucol monoester compounds (I) and (II) is claimed for  
 increasing high density lipoprotein (HDL) cholesterol level or improving  
 the functionality of circulating HDL.  
 DETAILED DESCRIPTION - Use of probucol monoester compounds of formula  
 T-linker-X (I) and T-linkera-O-SO<sub>2</sub>-OR<sub>4</sub> (II), their salts or prodrugs is  
 claimed for increasing high density lipoprotein (HDL) cholesterol level or  
 improving the functionality of circulating HDL.  
 T = a group of formula (i);  
 linker = (CH<sub>2</sub>)<sub>g</sub>Q(CH<sub>2</sub>)<sub>h</sub>;  
 linkera = (CH<sub>2</sub>)<sub>k</sub>, alkyl, lower alkyl, alkenyl, alkynyl, heterocyclyl,  
 aryl, heteroaryl, aralkyl, heterocyclylalkyl, heteroarylalkyl, alkaryl,  
 alkylheterocyclyl or alkylheteroaryl (all optionally substituted by at  
 least one OH, alkyl, lower alkyl, 1-5C alkoxy, halo, NO<sub>2</sub>, amino, CN,  
 aminocarbonyl, alkylamino or halo(1-5C)alkyl);  
 g = 1-3;  
 h = 0-3;  
 k = 1-10;  
 Q = O, S or CH<sub>2</sub>;  
 X = CH<sub>2</sub>COOR, COOR or CONR<sub>1</sub>R<sub>2</sub>;  
 R, R<sub>1</sub>, R<sub>2</sub> = H, alkyl, lower alkyl, aryl, aralkyl or alkaryl (all  
 optionally substituted by at least one OH, halo, alkoxy, carboxy or  
 amino), or  
 R<sub>1</sub> + R<sub>2</sub> = 4-8 membered ring;  
 R<sub>4</sub> = H, alkyl, lower alkyl, alkenyl, alkynyl, heterocyclyl, aryl,  
 heteroaryl, aralkyl, heterocyclylalkyl, heteroarylalkyl, alkaryl,  
 alkylheterocyclyl or alkylheteroaryl (all optionally substituted by at  
 least one OH, alkyl, lower alkyl, 1-5C alkoxy, halo, NO<sub>2</sub>, amino, CN,  
 aminocarbonyl, alkylamino or halo(1-5C)alkyl).  
 INDEPENDENT CLAIMS are also included for the following:  
 (1) new compounds (II), and;  
 (2) measuring the ability of a compound (preferably probucol  
 monoester) to increase the level of circulating HDL cholesterol which  
 comprises administering the compound to an animal (preferably mouse or  
 hamster) transfected with the human apo A-1 gene and measuring the  
 increase in human apo A-1 HDL.  
 ACTIVITY - Cardiant; Antiarteriosclerotic.  
 MECHANISM OF ACTION - None given in the source material.  
 USE - Used for increasing HDL cholesterol level, improving the  
 circulating functionality of HDL and treating cardiovascular diseases e.g.  
 atherosclerosis.  
 In an in vitro cell culture assay, HepG2 cells were cultured in  
 minimum essential medium containing 10% FBS, and streptomycin (100 mu  
 g/ml), penicillin (100 unit/ml) and glutamine (4 mM). Cells were grown for  
 2 days till they were 80% confluent in 6-well or 12-well plates before  
 studies. To measure apoAI, 96-well microtiter plates were coated with a  
 1:1000 diluted mixture of three monoclonal antibodies against human apoAI

for 2 hours and incubated in succession with HDL3 (0 - 15 ng/well), carboxymethoxyacetic acid, mono(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methyl-ethyl)-thio-2,6-bis(1,1-dimethylethyl)phenyl)ester (Ib) (test compound)/probucol (control compound), sheep polyclonal anti-apoAI serum, alkaline phosphatase-labeled rabbit anti-sheep and para-nitrophenyl phosphate (1 mg/ml in 10 mmol/l ethanolamine, 0.5 mmol/L MgCl<sub>2</sub>, pH 9.5), for 2, 1 and 1 hour respectively at 37 deg. C. The plates were washed three times between different incubations. The percentage increase apoAI HDL in HepG2 cells using the test compound/control compound was 47/-21.

ADVANTAGE - The probucol monoesters increase the (HDL-c) level and improve the functionality of circulating high density lipoprotein in a host, by increasing HDL-particle affinity for hepatic cell surface receptors or increasing the half life of apoAI-HDL by at least 20 (preferably 30, 40, 50 or 60)% without increasing serum LDLc levels or decreasing apoAI protein synthesis. The medicament increases the HDL holoprotein levels by decreasing the internalization and degradation of HDL holoproteins.

Dwg.0/7

FS

CPI

FA

AB, GI; DCN

MC

CPI: B01-C04; B01-D02; B03-H; B06-A01; B06-D01; B06-D11; B07-A02A; B07-A02B; B07-D04C; B07-D08; B07-D09; B07-D13; B10-A08; B10-A09A; B10-A13C; B10-A13D; B10-A15; B10-A17; B10-B03B; B10-C03; B14-F01; B14-F07

TECH

UPTX: 20030129

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation of (II) is given in the source material.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The method also comprises administering a statin comprising lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, mevastatin, velostatin, compactin, dalvastatin, fluindostatin, dihydrocompactin, rivastatin, SDZ-63,370, CI-981, HR-780, L-645,164, CL-274,471, alpha, beta and gamma tocotrienol, (3R,5S,6E)-9,9-bis(4-fluorophenyl)-3,5-dihydroxy-8-(1-methyl-1H-tetrazol-5-yl)-6,8-nonadienoic acid, L-arginine salt, (S)-4-((4-(4-fluorophenyl)-5-methyl-2-(1-methylethyl)-6-phenyl-3-pyridinyl)ethenyl)-hydroxy-phosphinyl)-3-hydroxy-butanoic acid, disodium salt, BB-476, (British biotechnology), dihydrocompactin, (4R-(4-alpha, 6beta(E)))-6-(2-(5-(4-fluorophenyl)-3-(1-methylethyl)-1-(2-pyridinyl)-1H-pyrazol-4-yl)ethenyl)tetrahydro-4-hydroxy-2H-pyran-2-one or 1H-pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-beta,delta-dihydroxy-5-(1-methylethyl)-3-phenyl-4-((phenylamino)carbonyl)-calcium salt (R-(Rasterisk,Rasterisk)).

The method also comprises administering a fibric acid derivative comprising clofibrate, fenofibrate, ciprofibrate, bezafibrate or gemfibrozil.

The method also comprises administering a saturated phytosterol or stanol comprising campestanol, cholestanol, clionastanol, coprostanol, 22,23-dihydro-brassicastanol, epicholestanol, fucostanol or stigmastanol.

The method also comprises administering a diuretic comprising hydrochlorothiazide, chlorothiazide, furosemide, bumetanide, ethacrynic acid, amiloride, triameterene, spironolactone, **eplerenone**, acetazolamide, althiazide, amanozine, ambuside, amiloride, arbutin, azosemide, bendroflumethiazide, benzthiazide, benzylhydro-chlorothiazide, butazolamide, buthiazide, chloraminophenamide, chlorazani, chlorthalidone, clofenamide, clopamide, clorexolone, cyclopenthiazide, cyclothiazide, disulfamide, epithiazide, ethiazide, ethoxolamide, etozolin, fenquizon, furosemide, hydrazacarbazine, hydrochlorothiazide, hydroflumethiazide, indapamide, isosorbide, mannitol, mefruside, methazolamide, methyclothiazide, meticrane, metochalcone, metolazone, muzolimine, paraflutizide, perhexiline, piretanide, polythiazide, quinethazone, teclothiazide, ticrynaf, torasemide, triamterene, trichlormethiazide, tripamide, urea or xipamide.

The method also comprises administering an antihypertensive agent comprising an andrenergic blocker, a mixed alpha/beta andrenergic blocker, an alpha andrenergic blocker, beta andrenergic blocker, an andrenergic stimulant, an angiotensin converting enzyme (ACE) inhibitor, an angiotensin II receptor antagonist, a calcium channel blocker, a diuretic or a vasodilator. The andrenergic blocker comprises phenoxybenzamine, guanadrel, guanethidine, reserpine, terazosin, prazosin or polythiazide. The andrenergic stimulant comprises methyldopa, methyldopate, clonidine, chlorthalidone, guanfacine, guanabenz or trimethaphan. The alpha/beta andrenergic blocker comprises carvedilol or labetalol. The beta andrenergic blocker comprises propranolol, metaprolol, acebutol, alprenol, amosulal, arotinolol, atenolol, befunolol, betaxolol, bevantolol, bisoprolol, bopindolol, bucumolol, bufetolol, bufuralol, bunitrolol, buprandolol, butiridine hydrochloride, ebutofilolol, carazolol, carteolol, carvedilol, celiprolol, cetamolol, cloranolol, dilevalol, epanolol, indenolol, labetalol, levobunolol, mepindolol, metipranolol, **metoprolol**, moprolol, nadolol, nadoxolol, nebivalol, nipradilol, oxprenolol, perbutolol, pindolol, practolol, pronethalol, propanolol, sotalol, sufinalol, talindol, tertatolol, tilisolol, timolol, toliprolol or xibenolol. The alpha andrenergic blocker comprises doxazosin and phentolamine, amosulalol, arotinolold, apiprazole, doxazosin, fenspiride, indoramin, labetalol, naftopidil, nicergoline, prazosin, tamsulosin, tolazoline, trimazosin or yohimbine. The angiotensin converting enzyme inhibitor comprises quinapril, perindopril, erbumine, ramipril, captopril, fosinopril, trandolapril, lisinopril, moexipril, enalapril, benazepril, alacepril, ceronapril, delapril, imadapril, moveltopril, spirapril or temocapril. The angiotensin II receptor antagonist comprises candesartan cilexetil, inbesartan, losartan, valsartan or eprosartan. The calcium channel blocker comprises verapamil, diltiazem, nifedipine, nimodipine, delodipine, nicardipine, isradipine, amlodipine, bepridil, clentiazem, fendiline, gallopamil, mibefradil, prenylamine, semotiadil, terodiline, verapamil, aranipine, bamidipine, benidipine, cilnidipine, efonidipine, elgodipine, felodipine, isradipine, lacidipine, lercanidipine, manidipine, nicardipine, nifendipine, nilvadipine, nimodipine, nisoldipine, nitrendipine, cinnarizine, flunarizine, lidoflazine, lomerizine, bencyclane, etafenone or perhexiline. The vasodilator comprises hydralazine, minoxidil, diazoxide, nitroprusside, aluminum nicotinate, amotriphene, bamethan, bencyclane, bendazol, benfurodil hemisuccinate, benziodarone, betahistine, bradykinin, bovincamine, bufeniode, buflomedil, butalamine, cetiedil, chloracizine, chromonar, ciclonicate, cinepazide, cinnarizine, citicoline, clobenfuril, clonitrate, cloricromen, cyclandelate, diisopropylamine dichloroacetate, dilazep, dipyrindamole, droprenilamine, ebumamonine, efloxate, eledoisin, erythrityl, etafenone, fasudil, fendiline, fenoxedil, floredil, flunarizine, ganglefene, hepronicate, hexesterol, hexobendine, ibudilast, ifenprodil, iloprost, inositol, isoxsuprine, itramin tosylate, kallidin, kallikrein, khellin, lidofiazine, lomerizine, mannitol, hexanitrate, medibazine, moxislyte, nafronyl, nicametate, nicergoline, nicofuranose, nimodipine, nitroglycerin, nylidrin, papaverine, pentaerythritol tetranitrate, pentifylline, pentoxifylline, pentrinitrol, perhexilline, pimefylline, piribedil, prenylamine, propatyl nitrate, prostaglandin EI, suloctidil, tinofedrine, tolazoline, trapidil, tricromyl, trimetazidine, trolnitrate phosphate, vincamine, vinpocetine, viquidil, visnadine or xanthinol niacinate.

The method also comprises administering a cholesteryl ester transfer protein inhibitor comprising (-)-(2R,4S)-4-amino-2,2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester.

ABEX

UPTX: 20030129

SPECIFIC COMPOUNDS - The use of four compounds (I) i specifically claimed e.g:

pentanedioic acid, mono(4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenyl)ester (Ia).

One compound (II) is specifically claimed i.e:

4-(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenoxy)-4-oxo-1-butyl sodium sulfate (IIa).

ADMINISTRATION - The dosage is 0.1-500 (preferably 1-100) mg/kg/day orally, parenterally (including intravenously, intradermally or subcutaneously) or topically.

EXAMPLE - (4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenyl)-4-hydroxybutyrate (12.5 g) and sulfur trioxide trimethylamine complex (12.5 g) were dissolved in dimethylformamide (150 ml) and stirred at room temperature for 2 hours. It was evaporated under vacuum to give a residue which was dissolved in dichloromethane (100 ml). The solution was washed with water (2 x 30 ml) and evaporated. Chromatography (dichloromethane/methanol, 10:1, 5:1) gave 3-(4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenoxy)propyl hydrogen sulfate. Tetrahydrofuran (200 ml) was added to this compound, sodium hydroxide (0.8 g) in water (5 ml) was added and the mixture was stirred at room temperature for 2 hours. It was evaporated and then 1N NaOH (200 ml) was added and the mixture stirred for 30 minutes. The precipitate was filtered out and dried to give 4-(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenoxy)-4-oxo-1-butyl sodium sulfate (IIa) (9.23 g).

L92 ANSWER 2 OF 3 WPIX (C) 2003 THOMSON DERWENT  
 AN 2001-482984 [52] WPIX  
 CR 2000-170974 [15]  
 DNC C2001-144714  
 TI New biphenyl sulfonamides, useful as angiotensin endothelin receptor antagonists and for treatment of e.g. hypertension, atherosclerosis, asthma and ischemia.  
 DC B05  
 IN GU, Z; MACOR, J E; MURUGESAN, N; TELLEW, J E  
 PA (BRIM) BRISTOL-MYERS SQUIBB CO  
 CYC 93  
 PI WO 2001044239 A2 20010621 (200152)\* EN 286p C07D413-12  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE  
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
 LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK  
 SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2001020926 A 20010625 (200162) C07D413-12  
 EP 1237888 A2 20020911 (200267) EN C07D413-12  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI TR  
 ADT WO 2001044239 A2 WO 2000-US33730 20001213; AU 2001020926 A AU 2001-20926  
 20001213; EP 1237888 A2 EP 2000-984282 20001213, WO 2000-US33730 20001213  
 FDT AU 2001020926 A Based on WO 200144239; EP 1237888 A2 Based on WO 200144239  
 PRAI US 2000-643640 20000822; US 1999-464037 19991215; US 2000-481197  
 20000111; US 2000-513779 20000225; US 2000-604322 20000626  
 IC ICM C07D413-12  
 ICS A61K031-42; A61P009-12; C07D261-16; C07D401-12; C07D403-14;  
 C07D413-14; C07D417-12; C07D487-04  
 AB WO 200144239 A UPAB: 20021022  
 NOVELTY - Biphenyl sulfonamides (I), and their enantiomers, diastereomers, salts and metabolites, are new.  
 DETAILED DESCRIPTION - Biphenyl sulfonamide compounds of formula (I), and their enantiomers, diastereomers, salts and metabolites, are new.  
 R1 = a group of formulae (a) - (o);

R2 = T or aryloxy, provided that when R1 is a group of formula (b), that R2 is not H, halo, (halo)alkyl, alkoxy, hydroxyalkyl, nitro,  $-(CH_2)_wNR_{19}R_{20}$  or  $-NHSO_2R_{22}$ ;

T = H, halo, CHO, (halo)alkyl, alkenyl, alkynyl, (halo)alkoxyalkyl, (cycloalkyl)alkyl, alkoxyalkoxy, cyano, hydroxy(alkyl), nitro,  $-CH(OR_{13})(OR_{14})$  or  $-(CH_2)_wY$

R3 = heteroaryl;

R4, R5 = (hydroxy)alkyl, (hydroxy-substituted)cycloalkyl or (hydroxy-substituted)alkoxyalkyl; or

R4 and R5 together = cyclobutyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl or tetrahydropyranyl (all optionally substituted with one or more OH);

R6 = (hydroxy)(halo)alkyl, (hydroxy-substituted)(cycloalkyl)alkyl, aralkyl, (hydroxy-substituted)alkoxy(alkyl) or  $-NR_{16}R_{17}$ ;

R7 =  $-(CH_2)_w-CO_2R_{15}$ ,  $-(CH_2)_w-(C=O)NR_{16}R_{17}$ ,  $-(CH_2)_w-NR_{15}(C=O)NR_{16}R_{17}$ ,  $-(CH_2)_w-CH_2OH$  or  $-(CH_2)_w-(C=O)R_{15}$ , or tetrazolyl, oxadiazolyl or triazolyl (each optionally substituted with H, alkyl, OH or halo);

R8, R9, R9a, R10, R12 = H, halo, (hydroxy)alkyl, (cycloalkyl)(alkyl), (hetero)aryl, arylalkyl, alkylthioalkyl, alkoxy(alkyl); or

R11, R11a = H, alkoxy or together form a carbonyl;

R13, R14 = alkyl or together form a 5- or 6-membered ring;

R15, R16, R17 = H, (hydroxy)alkyl, (cycloalkyl)(alkyl), alkoxyalkyl, aralkyl, heterocycloalkyl, (hetero)aryl or  $-(CH_2)_wQ$ ; or

R16 and R17 together = 4-6 membered heterocyclic ring;

n = 1 or 2;

w = 0, 1 or 2;

Y = heteroaryl,  $-COOH$ ,  $-COOR_{18}$ ,  $-CONR_{19}R_{20}$ ,  $-NR_{19}-OR_{20}$ ,  $-NR_{21}(C=O)R_{22}$ ,  $-NR_{21}(C=O)NR_{19}R_{20}$ ,  $-N(R_{19})-(alk)-NR_{21}(C=O)R_{22}$ ,  $-NR_{21}(C=O)OR_{18}$ ,  $-NR_{21}SO_2R_{22}$ ,  $-SO_2R_{22}$ , or a group of formulae (q), (r) or (s);

R18 - R22 = H, (halo)alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (hetero)aryl or aralkyl; or

R19 and R20 together = 4-7 membered cycloalkyl ring;

R23, R24 = H, (cyclo)alkyl or together form a 3-7 membered ring;

Z = O,  $-N(R_{25})-$  or  $-C(R_{26})(R_{27})-$ ;

x = 2, 3 or 4;

R25, R26, R27 = H, (cyclo)alkyl or R26 and R27 together form a 3-7 membered cycloalkyl ring; and

R101 - R104 = T in which all (hetero)aryl rings are optionally substituted by H, halo, cyano, (hydroxy)alkyl, alkoxy, nitro or trifluoromethyl.

Provided that when R1 is a group of formula (a), (I) is not a compound of formula (II).

INDEPENDENT CLAIMS are also included for:

(1) a compound of formula (I) in which R3 = isoxazol-5-yl or isoxazol-3-yl (optionally substituted with 2 of alkyl or halogen, and R1 is any group such that the resulting compound demonstrates affinity (IC<sub>50</sub>) for both the AT<sub>1</sub> receptor and ETA receptor of less than 5 mM at both receptors

(2) a pharmaceutical composition comprising (I), at least one ACE inhibitor (such as captopril, zofenopril, fosinopril, ceranapril, alacepril, enalapril, delapril, pentopril, quinapril, ramipril, or lisinopril), vasopepsidase inhibitor (such as omapatrilat or gemopatrilat), HMG CoA reductase inhibitor (such as pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522), anti-platelet agent (such as clopidigrel, ticlopidine, CS-747 or aspirin), anti-diabetic agent (such as biguanides or biguanide/glyburide combinations), beta-adrenergic agent (such as carvedilol or **metoprolol**) or mineralocorticoid receptor antagonist (such as spironolactone or **eplerenone**).

ACTIVITY - Antiarthritic; nootropic; neuroprotective; antianginal; antiarrhythmic; antiarteriosclerotic; antiinflammatory; analgesic; cytostatic; cardiant; cerebroprotective; hepatotropic; dermatological;

ophthalmological; antidiabetic; antidiarrheic; anticonvulsant; vasotropic; litholytic; hemostatic; hypotensive; antimigraine; osteopathic; antipsoriatic; antiulcer.

MECHANISM OF ACTION - Endothelin receptor antagonist; angiotensin II receptor antagonist. Tests were carried out but no results are given.

USE - (I) are useful in the treatment of disorders related to renal, glomerular and mesangial cell function. For treatment of disorders related to paracrine and endocrine function. For treatment of endotoxemia or endotoxin shock or hemorrhagic shock. For alleviating pain associated with prostate and bone cancer. For preventing end-organ damage associated with the cell-proliferative effects of endothelin. For treatment of hypoxic and ischemic diseases (such as cardiac, renal and cerebral ischemia and reperfusion). As antiarrhythmic, antianginal, antifibrillatory, antiasthmatic, antiarteriosclerotic, and antidiarrheal agents. As adjuncts to thrombolytic therapy. For treatment of myocardial infarction, peripheral vascular disease (e.g. Raynaud's disease), cardiac hypertrophy, primary pulmonary hypertension, trauma, central nervous system vascular disorders (such as migraine, stroke and hemorrhage), central nervous system behavioural disorders, gastrointestinal diseases (such as Crohn's disease, ulcers and inflammatory bowel disease), pancreatitis and gall bladder disorders. For regulation of cell growth. For treatment of restenosis following transplantation. For therapy of congestive heart failure including inhibition of fibrosis. For treatment of sickle cell disease, liver disease, deleterious consequences of ET-producing tumors, spastic diseases of the urinary tract and bladder, hepatorenal syndrome, immunological diseases (including vasculitis) fibrosis associated with renal dysfunction, metabolic and neurological disorders, cancer, insulin-retinopathy, diabetes mellitus, neuropathy, retinopathy, epilepsy, bone remodelling, psoriasis, and chronic inflammatory diseases (such as arthritis, rheumatoid arthritis, osteoarthritis, sarcoidosis and eczematous dermatitis). For treatment of disorders involving bronchoconstriction. For treatment of sexual dysfunction, Alzheimer's, senile dementia and vascular dementia.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B05-B01E; B06-H; B07-D04B; B07-D09; B07-D13; B10-A08; B10-A17; B10-B02B; B10-C03; B14-C09; B14-E02; B14-E10; B14-F01; B14-F02B; B14-F02C; B14-F02D; B14-F03; B14-F07; B14-G02C; B14-G03; B14-H01; B14-J01; B14-J05D; B14-J07; B14-K01A; B14-K01D; B14-N01; B14-N13; B14-N16; B14-S06; B14-S07

TECH UPTX: 20010914

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be prepared by:

- (1) reacting a sulfonyl-substituted phenyl bromide with an phenyl boronic acid (or ester) to form a biphenyl sulfonyl compound;
- (2) converting the biphenyl sulfonyl compound into a biphenyl sulfonyl chloride; and
- (3) reacting the biphenyl sulfonyl chloride compound with an aryl amine.

ABEX UPTX: 20010914

SPECIFIC COMPOUNDS - Numerous compounds of formula (I) are specifically claimed including 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-fluoroethoxymethyl)(1,1'-biphenyl)-2-sulfonamide

ADMINISTRATION - Dosage is 0.1 - 100 (preferably 0.2 - 50, more preferably 0.5 - 25) mg/kg. Administration is by any suitable means.

EXAMPLE - 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-2'-formyl-N-(3,4-dimethyl-5-isoxazolyl)-(1,1'-biphenyl)-2-sulfonamide (110 mg, 0.20 mmol) in dichloromethane (4 ml) was added to 4-amino-2,2-dimethylbutanoic acid hydrochloride (98 mg, 0.59 mmol) and 3 angstrom molecular sieves, followed by glacial acetic acid (35 mg, 0.59 mmol) and then sodium acetate (48 mg, 0.59 mmol). The mixture was stirred for 8

minutes and NaB(AcO)3H (124 mg, 0.59 mmol) was then added. The reaction mixture was stirred for 2 hours at room temperature, diluted with ethyl acetate and filtered through celite. The filtrate was washed with water and brine, dried and concentrated.. This material was dissolved in dichloromethane (6 ml) and 1,3-diisopropylcarbodiimide (32 mg, 0.25 mmol) was added. The reaction mixture was stirred at room temperature for 2 hours, diluted with DCM, washed with water and brine, dried and concentrated. The residue was purified by preparative HPLC to provide 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-((3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl)(1,1'-biphenyl)-2-sulfonamide (40 mg, 31%), m. pt 104 - 110 degrees C.

DEFINITIONS - Preferred definitions:

R1 = a group of formulae (a), (e) or (g);

R2 = -CH2Y or (halo)(alkoxy)alkyl;

Y = a group of formula (q);

R3 = isoxazol-5-yl or isoxazol-3-yl (both substituted with two substituents selected from halo and alkyl); and

R101 - R104 = H, halo or alkyl.

L92 ANSWER 3 OF 3 WPIX (C) 2003 THOMSON DERWENT  
 AN 2000-317820 [27] WPIX  
 DNC C2000-096186  
 TI Treating weight loss due to cachexia which occurs in liver cirrhosis, cardiac cachexia involves administering an agent which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status.  
 DC B05  
 IN ANKER, S D; COATS, A J S  
 PA (IMCO-N) IMPERIAL COLLEGE INNOVATIONS LTD  
 CYC 21  
 PI WO 2000021509 A2 20000420 (200027)\* EN 72p A61K031-00  
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 W: JP US  
 EP 1121111 A2 20010808 (200146) EN A61K031-165  
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 JP 2002527378 W 20020827 (200271) 74p A61K045-00  
 ADT WO 2000021509 A2 WO 1999-GB3302 19991015; EP 1121111 A2 EP 1999-947762 19991015, WO 1999-GB3302 19991015; JP 2002527378 W WO 1999-GB3302 19991015, JP 2000-575485 19991015  
 FDT EP 1121111 A2 Based on WO 200021509; JP 2002527378 W Based on WO 200021509  
 PRAI GB 1999-17181 19990723; GB 1998-22458 19981015; GB 1998-22459 19981015  
 IC ICM A61K031-00; A61K031-165; A61K045-00  
 ICS A61K031-14; A61K031-167; A61K031-198; A61K031-403; A61K031-404; A61K031-4164; A61K031-4178; A61K031-433; A61K031-439; A61K031-485; A61K031-517; A61K031-56; A61K031-585; A61K031-663; A61K038-00; A61K038-55; A61K041-00; A61K045-06; A61P001-16; A61P003-10; A61P009-04; A61P009-12; A61P011-00; A61P013-12; A61P031-00; A61P031-18; A61P035-00  
 AB WO 200021509 A UPAB: 20000606  
 NOVELTY - Treating weight loss due to an underlying disease in a patient comprises administering an agent (I) which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status.  
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:  
 (1) treating weight loss due to an underlying disease in a patient which involves administering any one of the following compounds (III): a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a beta receptor blocker; an imidazoline receptor antagonist; a centrally acting alpha receptor antagonist; a peripherally acting alpha receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; scopolamine;



endothelin receptor antagonist; a xanthine oxidase inhibitor; or erythropoietin;

(2) treating weight loss due to underlying disease in a patient which involves electrically stimulating the patient's muscles;

(3) use of the above mentioned compounds in the manufacture of a medicament for preventing or treating weight loss due to underlying disease (idiopathic cachexia) or aging in a patient and also for manufacture of an agent for enhancing exercise performance in a healthy individual;

(4) preventing or treating weight loss due to the aging process in the patient which involves administering an agent (I) which reduces sympathetic nervous system activity, or (III);

(5) preventing or treating weight loss due to aging process which involves electrically stimulating the patient's muscles;

(6) enhancing exercise performance in a patient by administering (I) which reduces sympathetic nervous system activity, or (III);

(7) enhancing exercise performance in a patient by which involves electrically stimulating the patient's muscles;

(8) preventing weight loss consequent to a cardiovascular disorder in a patient at risk of heart disease which involves administering (III) with an inhibiting effect on aldosterone; a beta receptor blocker; an imidazoline receptor antagonist; a centrally acting alpha receptor agonist; a peripherally acting alpha receptor antagonist; or a ganglion blocking agent.

#### ACTIVITY - Anabolic.

The biological activity of (III) was tested in human cachexia patients. A patient with cachexia due to chronic heart failure (CHF) and a second patient with CHF and a muscle myopathy suffering from idiopathic cachexia were treated with 50 mg of an angiotensin II receptor antagonist (losartan) daily. The clinical status and parameters of body composition, strength and treadmill exercise capacity at base line and during follow-up was study for 126 days in patient 1 and 83 days in patient 2. The results showed that in both patients the exercise capacity was improved during the study. Also patient 1 had a weight gain of 4.6 kg.

MECHANISM OF ACTION - Sympathetic nervous system activator; Cardiac reflex status enhancer (claimed).

USE - The method is useful for treating weight loss in a patient having idiopathic cachexia with an underlying disease such as AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure (claimed).

Dwg.0/5

FS

CPI

FA

AB; DCN

MC

CPI: B01-B03; B01-C05; B04-A04; B04-C01A; B04-C01B; B04-C01C; B04-C01F; B04-N04B; B05-B01G; B06-A01; B06-A02; B06-A03; B06-D01; B06-D02; B06-D06; B06-D09; B06-D13; B06-F01; B06-F05; B07-A03; B07-D03; B07-D09; B07-D12; B07-E01; B07-E03; B07-F03; B09-B; B10-A13D; B10-A17; B10-A21; B10-B01A; B10-B02E; B10-B02F; B10-B02G; B10-B03B; B10-B04B; B14-E11; B14-J02C

TECH

UPTX: 20000606

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: Compound (I) which reduces the sympathetic nervous system activity is one of the compounds (III). The compound which inhibits the effect of aldosterone is any one of spironolactone, testolactone, RU40555, RU26752, canrenoate, **epplerenone**, 3-(17beta-hydroxy-3-oxoandrosta-1,4,6,11-tetraen-17alpha-yl) propionic acid gamma lactone, 3-(9-alpha-fluoro-7beta-hydroxy-3-oxo-androsta-4-en-17alpha-yl) propionic acid gamma lactone, dihydro-spirorenone, spirorenone, 15,16-methylene derivatives of spironolactone, mespirenone and SC9420. The chymase inhibitor is any one of alendronate, aprotinin and tissue inhibitors of matrix metalloproteinases. Cathepsin B inhibitor is any one of an epoxysuccinyl peptide such as CA-074 or E64-c, stefin A and cystatin C. beta-receptor

blocker is any one of acebutolol, alprenolol, atenolol, betaxolol, bisoprolol, carteolol, celiprolol, esmolol, labetolol, lavobunolol, metipranolol, **metoprolol**, nadolol, oxprenolol, penbutolol, pindolol, propanolol, sotalol, timolol, nebivolol, carvedilol and bucindolol. Imidazoline receptor antagonist is any one of moxonidine, rilmenidine, pentamidine and alpha-methyl DOPA. Centrally acting alpha receptor agonist is clonidine. Peripherally acting alpha receptor antagonist is any one of doxazosin, prazosin, terazosin and ipsapirone. Ganglion blocking agent is any one of azamethonium, dicolinium, hexamethonium, mecamlamine, pentamethonium, pentolinium, trimetaphan, benzo hexonium, hexafluorenum, cypenam, trimethaphan canfosulfonate, tetraethylammonium bromide and synapleg. Opiate is any one of dihydrocodeine, morphine, diamorphine and buprenorphine. ET-1 receptor antagonist is any one of butenolide, BQ123, BQ-788, A-216546, ABT-627, IRL3461, LU135252, S-0139, PD 142,893, PD 164333, RO 61-1790, PD 156,707, SB 209670, IRL 1038 AND WS-7338 B. Xanthine oxidase inhibitor is any one of allopurinol, 7,8-dihydroneopterin, 5,6,7,8-tetrahydrobiopterin, leukopterin, xanthopterin, neopterin, biopterin, 4-amino-6-hydroxypyrazolo(3,4-d)pyrimidine (AHPP) and oxypurinol.

ABEX UPTX: 20000606

ADMINISTRATION - Administration is through oral, parenteral injections, through inhalation, per-rectal and buccal routes. No specific clinical dosages are given.

EXAMPLE - No relevant example given.